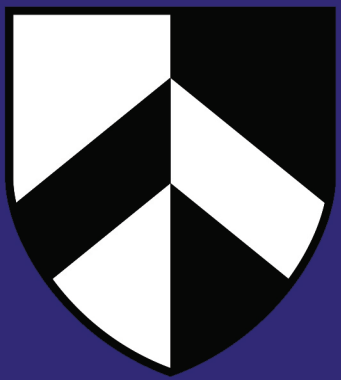
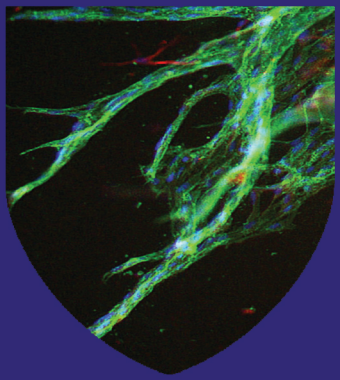
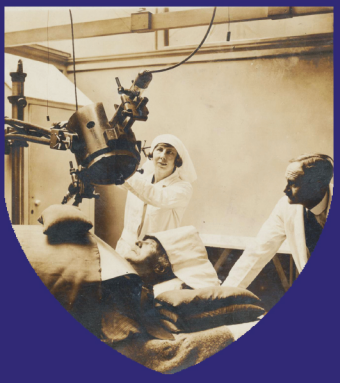
Every Rational Attempt

The Stories Behind Barts' Contribution to the Fight Against Cancer

Edited by Professor Nicholas Lemoine and Dr Delphine Purves

Every Rational Attempt:
The Stories Behind
The Contribution of Barts
In The Fight Against Cancer

Legend for the 'Shield' Cover Images:

Top row, L-R:

1. 1788 Portrait of Percival Pott (1714-1788) by George Rommey, displayed at the Hunterian Museum.

2. The St Bartholomew's Hospital Crest, which first became associated with the hospital in the 15th Century.

3. An aortic ring as seen through a microscope. Image captured by Dr Marianne Baker, Barts Cancer Institute.

Bottom row, L-R:

4. Sir Geoffrey Keynes with students, 1947. Courtesy of St Bartholomew's Hospital archives (X8/1502).

5. The entrance of the Queen Mary Charterhouse Square campus, home of the Barts Cancer Institute.

6. Radiotherapy to the jaw, c. 1929, Courtesy of St Bartholomew's Hospital Archives (SBHX8/180).

Dedicated to Staff and Students,
Past and Present, of the
Barts Cancer Institute

Every Rational Attempt:
The Stories Behind
The Contribution of Barts
In The Fight Against Cancer

Editors: **Professor Nicholas Lemoine**
Director

Dr Delphine Purves
Institute Manager

Editorial Assistant: **Mr Richard Le Vay**
Graduate Trainee

Barts
Cancer Institute
Queen Mary University of London

2015

First Printing: 2015

ISBN: 978-1-326-33764-3

Barts Cancer Institute, Queen Mary University of London
Old Anatomy Building, Charterhouse Square
London EC1M 6BQ

www.bci.qmul.ac.uk

"Every rational attempt toward relieving mankind from such an evil, will, I make no doubt, be favourably received…. for when the disease has got head, it is rapid in its progress, painful in all its attacks and most certainly destructive in its events".

Percival Pott, The Chirurgical Works of Percival Potts, FRS and Surgeon of St Bartholomew's Hospital, Volume 3, MDCCLXXIX (1779)

Contents

Foreword

"If I have seen further, it is by standing on the shoulders of giants", a much quoted phrase from one of the greatest scientists of all time, Isaac Newton (1675). Yet its sentiment remains as true today as it was then, that while great scientists are proud of their contributions to their field, they remain indebted to the scientists who preceded them, without whom they may never have been able to make that contribution.

And in this monograph about the impact of Barts on cancer medicine, you will see "giants" throughout, in the authors who have written of their time here, and in those they have written about. They were at the vanguard of what is now viewed as standard clinical practice and their unique talents changed the face of cancer treatment and understanding. The 20th century, particularly the latter half, was a time when a host of new weapons were discovered and produced in the so-called fight against cancer, pushing back the front line with revolutionary therapeutics, diagnostics, imaging and radiotherapy. In reading this monograph, it is clear that this was an extraordinary time and Barts, along with a handful of other institutions worldwide, was at the forefront of those discoveries.

Yet also evident from this monograph is the collegiality and camaraderie at Barts. It makes it a special place, for whom many who worked or still work here consider it a privilege to have done so. Anyone entering Barts for the first time, through the Gate and into the quadrangle, is struck by its beauty and serenity, and an almost tangible sense of its history, a story of human kindness and compassion. Begun in 1123 by the Augustinian monk, Rahere, he set up St Bartholomew's Hospital to provide solace to the sick, poor and dispossessed of London, offering them refuge, respite and care. Here it remains, arguably the oldest hospital in the world operating on the same site, still treating and caring for the sick, having fought off attempts to close it from Henry VIII to the UK government in the 1990s!

And this legacy of care is evident in this monograph in the memoires of those who have dedicated their professional lives to giving hope to cancer patients, by striving to overcome this most destructive of diseases through cutting-edge research and improvements in care – the same aims which continue to drive the current scientists now working at the Barts Cancer Institute (BCI). This monograph was commissioned to mark the end of the BCI's tenth anniversary

year, as a fitting tribute to all that has gone before, from many of those who were there at that time. It is daunting to consider the successes of the last ten years in the face of the triumphs summarised in this monograph, yet as Professor Hart has so eloquently described in his chapter, the discoveries continue to come, are being translated into very real patient benefits, and the dedication and calibre of the current scientists honour those on whose shoulders they now stand. From such a height, how much further can they see? Let us hope that they have the end in their sights and it will be this generation who will finally win the fight against cancer.

Dr Delphine Purves

Institute Manager, Barts Cancer Institute

CANCER-RELATED ACHIEVEMENTS AT BARTS

- **The idea that occupational exposure to environmental factors would cause cancer – Percival Pott, 1779**
- **The idea that cigarettes caused cancer – Ernest Kennaway, 1947**

- **First X-ray machine for clinical use - 1896**
- **Radiotherapy in head and neck cancer – Neville Finzi, 1907**
- **Local excision with radiotherapy to treat breast cancer – Geoffrey Keynes, 1922**
- **First radiotherapy department worldwide – Neville Finzi, 1924**
- **Use of super-voltage radiotherapy – Neville Finzi, 1936**

- **First UK Chair in Medical Oncology - Gordon Hamilton Fairley, 1971**
- **Sub-Specialty Recognition of Medical Oncology in the UK - Gordon Hamilton Fairley and Ronald Bodley Scott, 1975**
- **Cancer BACUP, a national patient support group, set up - Vicky Clement-Jones, 1985**
- **Introduction of the concept of MDT (multidisciplinary team) meetings in Haemato-oncology, Germ-Cell Tumour oncology (introducing teleconferencing in 1998) and Gynaecological Oncology, many years before their introduction nationally**

- **First retroperitoneal approach to radical excision of ovarian cancer – Christopher Hudson, 1967**
- **MVPP to cure Advanced Hodgkin's disease – Gordon Hamilton Fairley, 1975**
- **The effect of schedule on the activity of etoposide for lung cancer – Maurice Slevin and Simon Joel, 1999**
- **Department of Gynaecological Oncology established – John Shepherd, 1981**
- **MRI in Gynaecological Oncology to characterize adnexal masses, now adapted worldwide – Rodney Reznek and John Shepherd, 2004**
- **The concept of carboplatin as a single-agent therapy for testicular cancer - Tim Oliver, 2005**

AUTHORS' BIOGRAPHIES

Professor James Malpas

MB BSc D Phil FRCP FRCR FFPM FRCPCH

Professor of Medical Oncology and Director of the ICRF Medical Oncology Unit at Barts (1979 - 1995), James Malpas qualified from Barts in 1955 before joining the RAF for his National Service. In 1969, he was appointed Dean of the Medical College and in 1987, Vice President of the College. He is a highly distinguished researcher, notably in the fields of lymphoma, myeloma and children's cancer. Professor Malpas cemented his strong links with the local area through serving as Master of the Charterhouse from 1995-2000.

Dr Peter Wrigley

BM BCh PhD

Senior lecturer in the ICRF Medical Oncology Unit, having returned to Barts in 1966 as a Research Fellow and honorary senior registrar. He studied at University College London for his preclinical training before going to Oxford to join the Clinical Medical School at The Radcliffe Infirmary. In 1975, he took an NHS consultant job, a joint appointment between Barts and Hackney. He retired in 1995.

Professor Andrew Lister

MD FRCP FRCR FMEDSCI

Andrew Lister qualified from Cambridge and St Bartholomew's Hospital in 1969. Having been House Physician to Sir Ronald Bodley Scott, he was a research fellow at the ICRF Medical Oncology Unit and the Sidney Farber Cancer Institute, Boston, prior to joining the Staff of the Unit in 1977. He never left! He was Director and Professor of Medical Oncology from 1995-2010 and, for much of that time, also Director of Cancer Services and Clinical Haematology in Barts Health NHS Trust. He pursued the goal of improving the outcome of patients with haematological malignancy through working at the interface between the clinic and the laboratory.

Professor Ama Rohatiner

MD FRCP BA MRes

Professor of Haemato-Oncology at Barts until her retirement in 2010, Ama Rohatiner qualified at Guy's Hospital Medical School in 1974**.** After a year spent as Registrar, working with Dr. Peter Wrigley at the Solid Tumour Unit at Hackney Hospital, she became an ICRF Research Fellow in haematological malignancy at Barts, Her main research interest was the development of new treatment strategies for lymphoma. After her retirement, she studied and obtained a BA and MRes in English Literature.

Ms Jennifer Ellwood

SRN SCM

Jenny Ellwood was appointed Ward Sister in 1977 at the Hackney and Homerton Cancer Unit by Dr Peter Wrigley. She completed her nursing training at The London Hospital, before undertaking midwifery training in Edinburgh. She worked in Canada, nursing for several years, but returned to The London as Relief Sister. She was then appointed as the first London Hospital Sister to work in Mile End Hospital when it was taken over by The London during the reorganization of the National Health Service in 1970s. She remained at the Hackney and Homerton Cancer Unit until her retirement in 1997.

Dr Simon Joel

BSc PhD

Simon Joel, Emeritus Reader in Haemato-Oncology, joined Barts as a biochemist in Haemato-Oncology (formerly Medical Oncology) in 1982, becoming senior lecturer in 2002. He directed the Cancer Pharmacology group that conducts pharmacodynamic and pharmacokinetic studies of cytotoxic agents, against a background of clinical trials, and investigates the molecular pharmacology of novel agents. In addition to his research, Dr Joel was also the Postgraduate Teaching Lead for the Barts Cancer Institute, overseeing the academic development and progress of postgraduate students across the Institute. He retired in 2013.

Professor Sir John Lilleyman
LRCP MRCS MBBS FRCP FRCPath FRCPCH (Founder Fellow) DSc FMedSCi

Professor Lilleyman held the Ridgwell Chair of Paediatric Oncology from 1995-2004 at Barts, where he had qualified in 1968, returning in 1969 as a House Officer in Paediatrics. He was at Sheffield's Children's Hospital from 1975-1995, with a personal chair from 1993 in Paediatric Haematology. His career-long interest was in childhood leukaemia. He served as President of the Royal College of Pathologists from 1999-2002 and President of the Royal Society of Medicine from 2004-2006. In 2002, he was knighted for services to Pathology, the result of his efforts to establish the UK's system of Pathology lab accreditation.

Professor Tim Oliver
MD FRCP

Director of the Barts Male Genito-Urinary Unit until his retirement in 2006, Professor Oliver qualified in 1966 from Cambridge University, doing his research degree with Professor Hilliard Festenstein. He first became involved in cancer research at Barts in 1972, and from 1977 until 2006, his main work was in developing clinical trials and associated laboratory and epidemiology research in urological cancers, particularly testicular germ cell cancer and prostate cancer. He also helped to found Orchid, the UK's foremost male cancer charity, with a former patient, Colin Osbourne, in 1996.

Professor John Shepherd

FRCS FRCOG FACOG

Professor of Surgical Gynaecology from 1999, John Shepherd qualified at Barts, where he worked as a Consultant Gynaecological Oncologist from 1981. He served as the President of the Obstetrics and Gynaecology Section, Royal Society of Medicine (2006-2007), was appointed Hunterian Professor at the Royal College of Surgeons (2006-2007) and was President of the Society of Pelvic Surgeons (2007-2008). He moved to the Royal Marsden in 2008 as Consultant Gynaecological Surgeon.

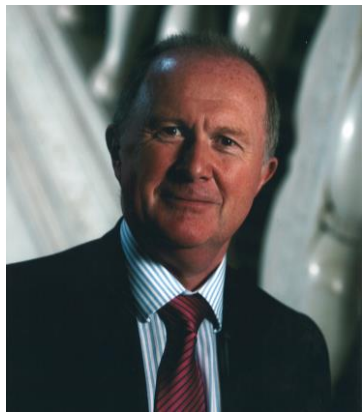
Professor Rodney Reznek

MA FRCP FRCR

In 1996, Professor Reznek was appointed Professor of Diagnostic Imaging at Barts, having joined as a consultant radiologist in 1983. He graduated from the University of Cape Town Medical School in 1972, and moved to the UK in 1975. In 1977, he began his training in Radiology at Barts. Over several decades, his research has focussed on the imaging of patients with gynaecological malignancy and those with neuroendocrine tumours He is co-founder and Past President of the International Cancer Imaging Society. He retired in 2011 and is currently studying History.

Professor Ian Hart

BVSc PhD MRCVS FRCPath, FRCP(Hon) FMedSci



Professor of Tumour Biology and Deputy Director of the BCI until his retirement in 2012, Professor Hart qualified in Veterinary Science before completing his PhD at the University of Bristol in 1976. He went to the lab of Dr Josh Fidler at the Frederick Cancer Center, Maryland. It was here that he began to focus upon tumour heterogeneity and the process of metastatic spread. In 1983, he was recruited by Sir Walter Bodmer as a Principal Scientist at the ICRF in Lincoln's Inn Fields where he headed the Biology of Metastasis Laboratory. From 1993–2003, he was the 'Richard Dimbleby Professor of Cancer Research' at St Thomas' Hospital.

Dr Nick Plowman

MA MD(Cantab) FRCP FRCR

Dr Nicholas Plowman is the Lead Consultant Clinical Oncologist at Barts Health NHS Trust and Head of Department since 1989. He qualified at Guy's Hospital in 1974. He has a long term interest in advances in the radiotherapeutic methods to treat prostate cancer and hormonal methods of therapy, and focused brain and body radiotherapy techniques (gamma and cyberknife). His demonstration of the importance of adrenal sex steroid production in both breast and prostate cancer and the therapies he pioneered have become standard treatment across the world.

Professor Nick Lemoine

MD PhD FRCPath FMedSci

Director of the Barts Cancer Institute since 2004, and Medical Director, National Institute of Health Research since 2014, Professor Lemoine trained at Barts and qualified with the London Gold Medal in 1983. He specialised in Pathology and Oncology. He was Professor of Molecular Pathology at Imperial College London, where he was Director of the Cancer Research UK Molecular Oncology Unit and the first Director of the National Translational Cancer Research Centre at Hammersmith Hospital. His research focuses on the molecular genetics of cancer and gene therapy.

The Medical Oncology Unit at St Bartholomew's Hospital

James Malpas
Professor Emeritus, Medical Oncology

Peter Wrigley
Retired Physician in Medical Oncology

Andrew Lister
Professor Emeritus, Medical Oncology

Founding the First UK Medical Oncology Unit – James Malpas

The Medical Oncology Unit at St Bartholomew's Hospital was the practical result of the idea of carrying out clinical cancer research and scientific enquiry in a clinical setting, and was a concept initiated by Michael Stoker (later Sir Michael Stoker), Director of research at The Imperial Cancer Research Fund (ICRF). As Dean of the Medical College in 1971, James Malpas was asked by the secretary of the Medical College, Cecil Morris and Sir Eric Scowen, to sign the letter proposing to the University of London that the College should establish the first Chair in Medical Oncology in Britain at St Bartholomew's Hospital with an endowment of £250,000. Gordon Hamilton Fairley was elected to the Chair shortly afterwards. Gordon was already a consultant physician at Barts. As a junior consultant, he had fifteen beds on Dalziel and Annie Zunz wards, but with twenty-five beds under the charge of the Queen's Physician, Sir Ronald Bodley Scott, the unit was clinically viable.

A small laboratory had been constructed close to the wards as a result of the enterprise of John Matthias, but space was very limited and one of the purposes of the new unit was to encourage better facilities for research on cancer close to the wards. Sir Eric Scowen, as Professor of Medicine at Barts and also Chairman of the ICRF, was ideally placed to negotiate an initial endowment of £250 000 and to increase it later to £500,000 to provide the salary of the Professor and full supporting staff.

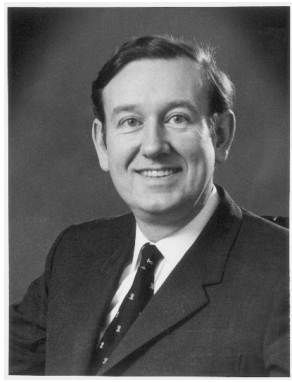
Gordon Hamilton Fairley and Sir Rodney Bodley Scott were able to have Medical Oncology recognised as a sub-specialty of general internal medicine. Gordon persuaded the Royal College of Physicians, which at that time was probably one of the most conservative bodies in medicine, to promote Medical Oncology as a specialty. This was an important move as it made training in the sub-specialty legitimate. On his return from an earlier visit to the USA, Gordon had introduced a variant of the treatment for disseminated Hodgkin's disease, a hitherto fatal condition, based on the mustine oncovin (vincristine), procarbazine and prednisolone regimen. By using vinblastine instead, vincristine's side–effects were reduced without affecting efficacy. MVPP was highly successful with excellent remission rates of 80% in patients previously untreated, or not previously treated with chemotherapy.

In the middle of the twentieth century, the outlook for patients with acute myeloblastic leukaemia was indeed dismal. Sir Ronald Bodley Scott, in his Lettsonian Lecture, had tried to dispel the nihilism that surrounded the dread disease. He said "*Although the outlook is bleak, the use of active drugs must be attempted in order to achieve remission of the disease, a nihilistic approach would produce an impenetrable barrier against therapeutic advance*".

He, therefore, encouraged the investigation of drugs such as rubidomycin, daunorubicin and cytosine arabinoside. Combination chemotherapy had been shown to be successful in acute lymphoblastic leukaemia in children treated in the USA. Sir Ronald and Derek Crowther, later to be professor of Medical Oncology in Manchester, developed a combination regimen for myeloblastic leukaemia. It may be apocryphal, but it has been said that they devised a combination of cytosine arabinoside and daunorubicin on the back of an envelope during a coffee break during a ward round! Whether this was true or not, the regimen was very successful with 58 of the first 72 patients treated achieving a complete remission compared with the usual meagre 20%. This treatment was rapidly brought into clinical practice and became the gold standard for the treatment of acute myeloblastic leukaemia. It was adopted by the Medical Research Council. It could be considered as one of the most significant and original contributions to cancer care by the Unit.

Professor Gordon Hamilton Fairley

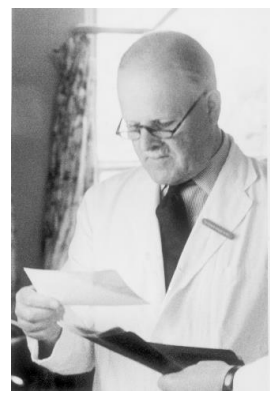
MA BMB Ch MRCP DM



The first Professor of Medical Oncology in England, at Barts until his untimely death, was killed by an IRA terrorist bomb in London on October 23, 1975 at the age of 45. He was instrumental in Medical Oncology becoming a recognised sub-specialty by the Royal College of Physicians in the UK. In 1970, he became director of the newly created Medical Oncology Research Unit, and in 1972 he was named, as Imperial Cancer Fund Professor of Medical Oncology, to the first chair of medical oncology to be established in England. By the time of his death, he had acquired a world-renowned status in his field and a reputation as a captivating lecturer. As a former student once wrote *"Gordon always generated excitement and when you were with him he made you feel clever, confident, better than you really were."*

Professor Sir Ronald Bodley Scott

GCVO KCVO BA Oxon BM BCh DM MRCP FRCP



Founder of Medical Oncology at Barts, physician to King George VI and Queen Elizabeth II, master of the society of Apothecaries. After studying natural sciences at Oxford, he graduated in medicine at Barts in 1931. After the Second World War, he developed his research interests in leukaemia and lymphoma. A notable achievement of Sir Ronald was successful introduction of drug treatments for myeloblastic leukaemia. He was determined to challenge what had been a "nihilistic" attitude towards haematological malignancies, and his work with Gordon Hamilton Fairley and others achieved dramatic increases in survival rates for chronic conditions such as Hodgkin's disease.

Success brought with it a number of problems. Although relatively well provided with beds at the beginning, when Sir Ronald retired in 1971, there began an acute shortage. Borrowing beds on other wards was unpopular and resented by other consultants. Secondly, the use of experimental new drugs, which were expensive, had a bad effect on the Hospital's drug budget, again upsetting the other clinicians.

During the 1970s, there were two major developments associated with the unit at Barts. The first was the formation of a Regional Cancer Unit at Hackney (see Jenny Ellwood's contribution), with joint appointments between the two hospitals. This was not without opposition from the local clinicians. Its main purpose was to treat the 'solid tumours', breast cancer, lung cancer and cancers of the gastrointestinal tract. A major contribution was the study of the pharmacology of morphine and its analogues (see Simon Joel's contribution). Fundamental findings were made on the metabolism of morphine. Etoposide or VP 16-213 was also studied and, with better knowledge of its metabolism, its efficacy was improved. These studies which were recognised nationally and were supervised by Peter Wrigley and Maurice Slevin.

A second development in the 1970s was in childhood cancer. For many years, I G Williams had treated children from Great Ormond Street Hospital with radiotherapy on Kenton Ward at Barts. Radiotherapy was regularly given to the renal bed of children who had had a nephrectomy for Wilms' tumour. Other childhood tumours were also treated. There was also a large practice in retinoblastoma, originating with H B Stallard of Olympic running fame and later Michael Bedford (see John Lilleyman's contribution).

Chemotherapy was being successfully used in an adjuvant setting in childhood tumours and dramatic improvements in acute leukaemia and lymphoma were beginning. This needed a redistribution of resources and Gordon Hamilton Fairley asked James Malpas if he would undertake the care of the children admitted to Barts with cancer. With the help and encouragement of Professor Donald Pinkel of St Jude's Children's Cancer Research Hospital in the USA, James Malpas was able to introduce the "Total Therapy" concept, which resulted in a number of papers recording success in, for example, rhabdomyosarcoma. Of eleven children with regional disease, eight remained well with no evidence of tumour some four to thirty-six months after diagnosis. This improvement was confirmed in later, larger studies. It was soon evident that, with these rare tumours, cooperation between hospitals was necessary.

This led to the formation of the Children's Solid Tumour Group with the Royal Marsden Hospital and, subsequently, with Great Ormond Street Hospital (GOSH). Important collaborators included Professor Tim McElwain, who in 1971 was appointed Consultant Physician and Senior Lecturer in Medicine at the Institute of Cancer Research and Royal Marsden Hospital, and Dr Jon Pritchard, Consultant Paediatric Oncologist and Senior Lecturer at Great Ormond Street and Institute of Child Health from 1976.

The Barts Unit was a founder member of the United Kingdom Children's Cancer Study Group, set up in 1977, which eventually served the whole country. Because a number of the children were referred from distant parts of the country a problem arose with caring for their relatives. Jon Prichard from Great Ormond Street hospital and James Malpas solved this by setting up The Sick Children's Trust, caring for parents and siblings in custom-built accommodation on the GOS site and Barts.

On the 23rd October 1975, Gordon Hamilton Fairley was killed by an IRA bomb planted beneath the car of his next door neighbour. The explosion occurred in the early morning. The news spread rapidly, but many of us in the Department could not believe it was true. Working in the clinic that morning we were confronted by a tearful Anthea Davies, Gordon's PA, who convinced us that the news was true. Michael Whitehouse, later to be Professor of Medical Oncology at Southampton University and currently Senior Lecturer, took over the academic duties and, with his usual efficiency, steadied our nerves. The College Committee decided to advertise the vacancy. There were a number of applications but no appointment was made and the matter went into abeyance. Professor Sir Eric Scowen asked James Malpas if he would take over the Directorship until such time as a decision was made on the Chair. This interregnum was to last five years until, in 1979, James Malpas was appointed to the Chair and, almost immediately, left for a visiting professorship in Australia at the invitation of Professor Henry Ekert.

During the eighties, with the rapid expansion of the childhood cancer work, it soon became evident that the facilities on Kenton ward were inadequate. As a result of an appeal, over £4 million was raised, without any help from fundraising organisations, and a new Paediatric Oncology unit, with separate facilities for adolescents, rooms for the administration of radioisotopes and bone marrow transplantation, was ready by July 1989. Major improvements in the treatment of the ocular tumour retinoblastoma were introduced by Adrian

Harnett, Judith Kingston and Nick Plowman. This was acknowledged by the Department of Health, who funded the first national centre for retinoblastoma at Barts. The centre developed external beam radiotherapy for retinoblastoma and pioneered combined radiotherapy and chemotherapy for intraocular retinoblastoma (see Nick Plowman's contribution).

The careful collection of clinical data and patients' samples had always been a feature of the unit's work ever since Gordon Hamilton Fairley's time. Nowhere was this more important than in the study of multiple myeloma, an inevitably fatal condition with a poor median survival. Using a meta-analysis of published series, James Malpas, Michael Richards and Walter Gregory showed that, at that time, multiple drug regimens were little better than melphalan and prednisolone. This encouraged us to try the high-dose melphalan supported by autologous bone marrow transplantation, introduced by the Royal Marsden Hospital, with which we subsequently ran a joint clinical programme. A 50% complete remission rate was achieved followed by a significantly increased survival.

In 1985, the Dean of the Medical College requested a report detailing why Barts should be recognised by the Regional Health Authority as a centre for the treatment of cancer. Coopers and Lybrand, a major Accountancy firm, were very helpful in providing data based on the Barts' experience. The report was presented by James Malpas, discussed at College Committee and Medical Council, and then submitted to the Regional Health Authority, who agreed that Barts should become recognised as a Regional Centre. This decision was of fundamental importance as the health service developed between 1985 and 1991 and, in 1992, may have influenced the newly-formed Trust to centre cancer treatment at Barts.

By the early 1990s, Barts had achieved a high reputation for the treatment of leukaemia and lymphoma. The Children's Oncology Unit was the fourth biggest in the country. It is, therefore, astonishing that, in 1992, the Conservative government tried to close Barts. Prompted by erroneous data from the King's Fund, they decided that there were too many teaching hospitals in London. Under the aegis of the then Secretary of State for Health, Virginia Bottomley and with the advice of an erstwhile Professor of Pathology from Newcastle, Bernard Tomlinson, the Westminster Hospital and the Middlesex Hospital were closed. Barts would have followed suit if it had not been for a determined stand by everyone concerned and the eventual *volte face* by a change

in Government.

Development of the Unit: Solid Malignancies – Peter Wrigley

The integration of the various ways to treat solid tumours was slower than the development of the treatment of leukaemia and lymphoma. A number of surgeons had used single cytotoxic drugs for some time, but mainly for just occasional cases, rather than in a planned way with strict protocols for the selection of patients, the choice of investigations to stage the disease, and then a programme of differing approaches depending on the findings. Gradually more and more cases of a variety of types of cancer were being referred to the Department from around the hospital. When Sir Ronald retired in about 1973, the number of beds available halved because he was replaced by a specialist in diabetes.

We had had beds on the first floor of the King George V block (Harvey and Luke Wards) where Sir Ronald worked, and also on the third floor (Dalziel and Annie Zunz Wards) where Gordon Hamilton Fairley admitted patients. As a consequence of this reduced number of beds directly available to us, we had to use beds all around the hospital .We tried to admit the most seriously ill patients to the third floor but this was not always possible.

Two teams were set up under Gordon Hamilton Fairley and James Malpas (Dean of the Barts medical school at the time and thus not able to be wholly involved in clinical work). Michael Whitehouse (ICRF fellow and hon. senior registrar) and Andrew Lister (ICRF Research Fellow and hon. registrar) looked after the main wards of Dalziel and Annie Zunz, while Peter Wrigley was the other hon. senior registrar/ICRF fellow looking after the patients in the rest of the hospital, including the children with cancer and leukaemia. This team had two doctors of senior house officer status. A consultant ward round of all the different wards took place twice a week and could take several hours.

About this time, James Malpas began a weekly outpatients clinic at St Leonard's Hospital in Shoreditch for general cancer problems and a monthly clinic in Chelmsford, Essex. More and more patients were being referred from these clinics and elsewhere, but bed space on the Barts site for their investigation and treatment was becoming an even greater problem. The link with Hackney Hospital was gradually growing closer. Two linked NHS consultant posts were created. James Malpas was appointed to the first in 1973. Two wards on the first floor of "B" block were identified for the proposed new unit in Hackney Hospital. They had to be converted for our use; the Dawn Trustees provided

much of the money for the building work. Peter Wrigley was appointed to the other consultant post in May 1975. There was a delay in equipping the wards such that the first patients were admitted in November 1975. The Wards were named "Bodley Scott" and "Hamilton Fairley"

The arrangement for each ward was largely open plan with two side rooms on each ward. The office for the collection of data was on the ward with two chartists keeping the details of the patients, and their treatment, in longhand form before computers were available. Peter Wilson and his assistants were invaluable. We were fortunate in persuading the administration to let us have a "housekeeper" for the wards. This sort of position had been eliminated in streamlining of wards in the 1970s. We appointed Mrs. Renée Smith, a local lady of firm authority who would be the mainstay of the Unit at Hackney Hospital, and then in Homerton Hospital, until the whole unit moved back to the Barts site in 1994. Mrs Smith and the nursing sisters, Jenny Ellwood and Christine White, were so important in the success of the Unit; they were part of the Unit for so many years. The office staff of Pat Jacobson and Julie Barlow provided a sure footing for all our work.

The Hackney Unit was very fortunate in the high quality of medical staff it attracted, which allowed us to plan and run complicated but effective treatment programmes. Drs. Hugo Baillie Johnson and Chris Collis were the first there and both went on to have distinguished careers as clinical oncologists. Drs. Ama Rohatiner and Maurice Slevin joined the department in Hackney in 1978. Maurice stayed to be the moving force in the development of the Unit in the Homerton Hospital. Ama went to the Barts site, remaining there to be the joint head of the leukaemia/lymphoma programme (see Ama Rohatiner's contribution).

Laboratory research was moved from Barts to the Homerton site, when we crossed the Homerton High Street from Hackney Hospital to the brand new Homerton Hospital in 1986. The new ward – Hamilton Fairley- was the first ward to open in the brand new hospital. It was so new there was no staff canteen; the nurses had to bring sandwiches from home for their lunch!

A large upper floor in one of the remaining old fever hospital buildings was converted for a clinical pharmacology unit. Dr Simon Joel led the research team directed by Maurice Slevin. Work was done on VP16-213, morphine and a number of other compounds, detailed in Simon's chapter.

Psychological research studies on the Unit were led by Dr Mary Cody. Nutrition was another new field of research, in association with the University of Surrey. Among those who were students was Susan Jebb (nee Parkinson) now Professor of Diet and Population Health at Oxford University. In 1992, the old building was due to be demolished and, with it, the site for our research; Mrs Norah Reed decided to raise the £80,000 needed, in memory of her husband Barry. It was planned to convert a terraced house belonging to the hospital into the lab. She set about the fundraising with vigor. She has been raising money for this research laboratory ever since! When the clinical Unit moved back to the Barts site, the research laboratory moved back to 38 Little Britain to be alongside the Hospital. The terrace house was never converted for our use.

The key to any treatment is the being sure of the histological diagnosis. We always reviewed the original microscope slides and, where possible, obtained the original paraffin blocks or if necessary took another biopsy before recommending a particular treatment plan. Once a week Dr Lowe from the pathology department listened to the clinical story, and then discussed the diagnosis while presenting the appearance of the biopsy material. A review of the patients' X-rays with Dr L Lessof on the following day developed the fuller picture of the extent of the disease, allowing a "stage" for the disease to be assigned from which the plan of treatment was made. Dr Rodney Reznek (now Professor) was always willing to fit our patients into the busy timetable of the CT scanner and later the MRI scanner. These careful reviews often altered our approach to the patient's problem - a change of interpretation of the diagnosis or the extent of the disease changing the whole management plan.

The patients set up a support group raising funds for the Unit. This was led by Fred Horne and Bob Cole. They called it the Daffy Duck Club. They purchased a lot of fluffy toy ducks which they sold for the Club. This was a thriving activity with Fred's cheerful voice often heard around the ward. Fred and Bob were both patients with myeloma. Derek Hack raised a lot of money for us by holding inter-club Amateur Boxing Association matches in Hemel Hempstead. He also had myeloma and received a bone marrow transplant on two occasions. Dirk Bogarde, the actor, performed a one man show at the Theatre Royal Haymarket to raise money for the Unit. The money raised by these men and the Daffy Duck Club enabled us to build a conservatory onto the ward which was opened by Mrs Daphne Hamilton Fairley on May 1992. It was a lovely hot summer's day.

A national support service grew from the idea of one of our patients, who was herself a doctor at Barts. Vicky Clement Jones's concept was that an expert telephone consultation should easily be available. BACUP (British Association

of Cancer United Patients) was born. The name was subsequently changed to CancerBackup. The first office was adjacent to Barts in Charterhouse Street. Dame Mary Donaldson (the first lady Lord Mayor of London) was the President. Finance was important to establish BACUP. Vicky's father and Mr Brian Skinner in Jersey gave the money. Peter Wrigley asked Dirk Bogarde to make the Sunday charity appeal at 7:50am on behalf of BACUP on Radio 4. He agreed. It was the first occasion when credit card donations over the phone were accepted immediately after the transmission. Dirk Bogarde was there answering the phone as part of a team. It was a great success. Maurice Slevin was the driving force in the development of the support service, encompassing booklets and pamphlets on individual cancers, besides the telephone help, and became chairman of the board of trustees after Vicky's death. CancerBackup eventually had 20 specialist cancer nurses answering 70,000 calls a year, and hundreds of thousands of site-specific booklets on cancer were made available up and down the country. The website was visited by half a million unique visitors a month. In 2008, Macmillan Cancer Care suggested that the charities merge, which has now happened, and the service which started in a small office in Charterhouse Street is now available to all patients in the country at all stages of the cancer journey, in a way that would make Vicky Clement Jones proud.

Maurice organised a patient support group which met on a Thursday evening. It was moderated by one of the medical staff, almost always a consultant. Sister Angela gradually took to running these meetings. She is a medically qualified, Church of England nun who at that time was serving at St Saviour's Priory in Haggerston. It was a very successful venture. Psychiatric advice and support came from Dr. Ruth Seiffert and Dr Mary Cody.

At this time, increased specialisation within Medical Oncology was developing. We decided to split our interests while continuing to look after all the patients on the ward. Dr Tim Oliver (now Professor) advised on kidney, bladder and testicular cancers. He would come to Homerton to see the patients; we would carry out his plan of treatment. He was working at The London Hospital, formerly a separate hospital and medical school before the current amalgamation. However, Tim Oliver and his team were part of the Medical Oncology Department. Maurice Slevin supervised the programmes for lung, breast, and ovarian cancers, while Peter Wrigley had a major interest in stomach, bowel, sarcomas, and mesothelioma. In the 1990's, bone marrow transplantation began to be used in the treatment of myeloma. The patients were all treated at the Homerton while those with lymphoma or leukaemia were treated at Barts.

The British Stomach Cancer Group was formed with Peter Wrigley as the Honorary Secretary. It was based in Birmingham, where the Regional Cancer Registry under the direction of Dr John Waterhouse, with Miss Jean Powell having collected and collated the stomach cancer cases in their area. Mr Victor Brookes (surgeon) was the influential Chairman. In Hackney and then Homerton, we developed a strong relationship with the surgeons especially Mr John Chalstrey (later Lord Mayor of London and becoming Sir John Chalstrey).

Patients with mesothelioma were referred to us from time to time. There had been the Cape Asbestos factory down by the river Thames. One of the women patients described the air being as thick with asbestos dust as though it were snowing! Our interest was heightened when a case of adenocarcinoma of the lung, which responded well to 5-Fluorouracil (5FU,) turned out, on review, to be undoubtedly one of mesothelioma! In later times, we linked with Dr Robin Rudd at the London Chest Hospital over the management of these patients (He had worked at Barts on our wards Annie Zunz and Dalziel in time past).

Initially, cytotoxic drugs were used only in cases of widespread metastatic disease of adenocarcinoma of the colon and rectum, but then they came to be offered when smaller amounts of disease were left after surgery. We used 5FU as a single drug until we read of the added benefit of adding folinic acid to the programme. One of the first patients we treated had had his colonic tumour resected and some liver metastases removed by the surgeon, Mr. Harvey White. He was then given intravenous 5FU for 5 days once a month for six months. He lived for more than ten years and died of pneumonia in his 80s. Dr Peter Clark was a hon. senior registrar/ICRF Fellow in the Homerton Unit at about that time (now Professor and Consultant Medical Oncologist at Clatterbridge Cancer Centre, Merseyside). He helped devise a variation of the combination described by a French group of medical oncologists. We treated a series of patients with this programme of drugs and published the results.

Radiotherapy was delivered at Barts in West Smithfield under the direction of Dr S. Arnott. He had come from a consultant position in Edinburgh to Barts. There was a very friendly joint relationship with ready access to his expertise.

Barts and Homerton Hospitals were under the same management in those days. In the early 1990s, we were told we could not have a senior registrar "on call" at both Bart's and Homerton at the weekend. Because it takes thirty minutes or more to get from Barts to the Homerton by car (or longer on public or hospital transport), we were going to be dependent on the duty medical registrar. Unfortunately, this doctor might well be a psychiatrist or a geriatrician with no

experience of managing Gram-negative septicaemia or the other acute emergencies seen in Medical Oncology. With reluctance, we decided it was not going to be safe if we stayed at the Homerton. We moved the Unit back to Barts in West Smithfield in 1994.

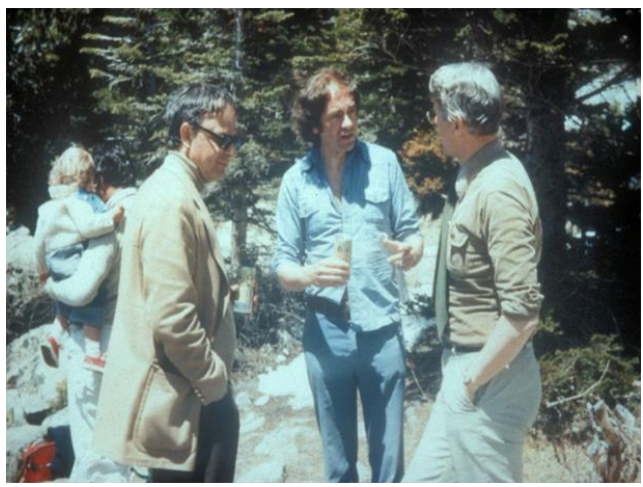
Development of the Unit: Haematological Malignancies - Andrew Lister

A critical initial goal of the ICRF Medical Oncology Unit (later CRUK), if not explicitly stated in 1970, was to improve the outcome of patients with haematological malignancy, and it remained so for the duration of its existence until it became the Centre for Haemato-Oncology in 2015. There is no doubt the goal remains the same today.

Against the background of magnificent nursing, diagnostic pathology and imaging, the large referral practice of patients with leukaemia, lymphoma and myeloma, historically to Sir Ronald Bodley Scott, provided the background to study and document the natural history of these invariably fatal diseases and the impact of therapy. The importance of the generosity of the ICRF and the foresight of its directors, particularly Walter Bodmer, despite the odd conflict, cannot be over-emphasised. Funding was renewed on the strength of a Quinquennial Review, unless performance was poor, for predominantly clinical academic staff. At a time when the NHS funded **no** specific positions for the nascent specialty of Medical Oncology, there were at least 4 research fellows on 4-year contacts, renewable for 1 year. During their period of tenure, it was expected that they would be honorary registrars/senior registrars, spending half their time on direct patient care and the other half on a research project towards an MD degree, usually based on observation, a clinical trial, and, early on, certainly quite amateur laboratory research. The opportunity to learn about the practice of medicine, and specifically Medical Oncology, was enormous, and the posts were very popular, attracting excellent candidates from near and far, many of whom have followed distinguished careers in Medical Oncology and Haematology.

As indicated, the challenge of changing the natural history of the haematological malignancies was addressed in a patient-oriented way, observing the illness, conducting clinical trials and, increasingly over time, by pursuing related research in the laboratory (immunological, pharmacological and molecular). To achieve this, the Barts resources were capitalised to a maximum by establishing long-standing collaborations, initially made possible through the close contacts and friendships which existed between Gordon Hamilton Fairley and colleagues at home and abroad. There were long-term

benefits from some of these collaborations, arising from the requirements of the particular projects, the significance of which were not recognised at the time. The clinical trial of immunotherapy for Acute Myeloblastic Leukaemia with the Royal Marsden Hospital (Ray Powles, Tim McElwain) demanded a tissue bank. The design of mathematical models for Hodgkin's Disease and Acute Leukaemia with Ray Jackson and his team in Operational Research at University College London (UCL), introduced by Alec Macdonald, led to Walter Gregory creating the clinical database. These two collaborations set the scene for the establishment of a system in which the routine storage of frozen tissue and the recording of all events in a patient's history, regardless of therapy, became the norm, only possible because of the ICRF grant. Similarly, the Cell Separator Unit, essential for the AML immunotherapy programme, but subsequently expanded for research into granulocyte and platelet transfusion, paved the way for the routine provision of platelets and the delivery of chemotherapy, staffed by senior nurses, all funded on the grant. It was not for at least 15 years that the NHS gradually took on the non-research aspect of the Unit's work, through the appointment of NHS medical and nursing staff in Medical Oncology.



George Cannellos, Derek Crowther and Jim Malpas at Little Bear Lake, during the ASCO meeting in 1977. In the background, Andrew Lister holding a young Sam Lister.

In the context of the initial ground-breaking trials in the Unit of the treatment of acute leukaemia and Hodgkin's Disease, examples of the value of potential 'informal' clinical collaboration are reflected in the clinical trials into the treatment of Hodgkin's Disease with the Christie Hospital (Manchester) through Derek Crowther and John Radford; of Acute Leukaemia with The

Ospedale Reuniti, Bergamo through Tiziano Barbui and Renato Bassan; and the establishment of the Unit at the forefront of investigating myelo-ablative therapy with autologous haematopoetic stem cell rescue for Follicular Lymphoma through collaboration with George Canellos, Lee Nadler and colleagues at the Dana Farber Cancer Institute, Boston.

Laboratory collaborations were likewise hugely rewarding. Until Gordon Hamilton Fairley's death, there was a weekly lab meeting held at the Institute of Cancer Research at Sutton, with Peter Alexander overseeing the possibility of immunotherapy trials. Collaboration with Mel Greaves, working originally in Av Mitcheson's Lab at UCL, led to the identification of the cALLA antigen (J5, CD10) in "common" Acute Lymphoblastic Leukaemia and to further research into the cell surface phenotype of lymphoid malignancy, the precursor of routine immunophenotyping. The collaboration was reciprocal - Barts provided clinical input and samples, and UCL, the laboratory expertise. There are many other examples including collaboration between the Unit at Barts and the Departments of Endocrinology at the Christie Hospital (Steve Shallot) and at Barts (Mike Besser, Lesley Rees) studying the challenge of infertility in relation to therapy, with Walter and Julie Bodmer at Lincolns Inn Fields studying the relevance of the HLA to Hodgkin's Disease.

The tissue bank and database also enabled the Unit to generate long-term data about the clinical course of the lymphomas and leukaemias and participate in major international projects – The International Prognostic Index, the Non-Hodgkin's Lymphoma Classification Project, and participation in the Leukaemia and Lymphoma Molecular Profiling Project (National Cancer Institute, US, Lou Stout) and The Lunenberg Lymphoma Biomarker Consortium (Anton Hagenbeek, Utrecht).

The productivity of collaboration as a consequence of our own resources is complemented by the enormous achievements of our own laboratory at Barts since the ICRF agreed to fund – again on the grant – a senior scientist. The recruitment of Brian Young, from the Beatson Institute in Glasgow, had an enormous long-term benefit to the Unit. Beyond establishing himself in the vanguard of research into the molecular pathogenesis of acute myeloid leukaemia, he raised the overall quality of research in the lab, attracting a succession of PhD students and postdoctoral fellows. With the re-organisation of the lab into individual but complementary groups, working in either myeloid or lymphoid malignancy, a new era began. Before leaving to take up a post in Ireland, Raj Gupta recruited Jude Fitzgibbon to work on Follicular Lymphoma (as well as aspects of acute leukaemia). Jude is now in the forefront of the field

himself, elucidating the pathogenesis of Follicular Lymphoma, and it is a pleasure to record that he now holds, among others, two programme grants of his own.

During the time since it first opened, the Medical Oncology Unit has evolved from a 90% clinical research group - observing diseases and conducting innovative clinical trials with limited in-house research, funded exclusively by ICRF then CRUK - into an organisation in which, in the new Centre for Haemato-Oncology, led by John Gribben, internationally appreciated lab research complements excellent patient care and participation in major clinical trials, in conjunction with National Health Service clinicians.

The life of the Medical Oncology Unit, as it was, lasted about thirty years during which all who worked in it were privileged to enjoy contributing to the exciting advances made worldwide at the time. There was no lack of challenges. The first five years saw the appointment of Barts' charismatic first senior lecturer Derek Crowther to the first CRC Chair of Medical Oncology in Manchester in November - Barts' loss, Manchester's gain; the appalling death of Gordon Hamilton Fairley, tragic both from the personal and the professional point of view; and the appointment of Barts' second senior lecturer, Mike Whitehouse, to the CRC chair of Medical Oncology in Southampton. The disruptions which followed - compounded by the uncertainty created by the Medical School's inability to replace Gordon Hamilton Fairley (not just once but twice!), the upheaval of the merger with the Royal London Hospital and the redistribution of services between the two hospitals, and the merger of the ICRF with CRC to form CRUK - did not prevent Jim Malpas taking the Unit forward in a wonderfully rewarding time to be in the field. Mostly great fun!

And the way was paved for the role of the current Centre for Haemato-Oncology in the Barts Cancer Institute.

Haemato-Oncology

Ama Rohatiner
Professor Emeritus, Haemato-Oncology

Forgive me for starting like a schoolgirl writing an essay, by recounting my first day at Barts in 1978: expectantly, I approached 'the Square'; its perfect symmetry both beautiful and impressive. My appointment as Registrar was actually at the Medical Oncology Unit at Hackney Hospital, but it had been suggested (or decreed, I shall never know), that I spend the first three months working at Barts. I was looking forward to it, apart from worrying that I had no experience of looking after people with haematological malignancy.

My first consultation in the Clinic seemed to be going well when I was called to the phone, 'Where are you? You're half an hour late!' No apology or explanation on my part seemed to appease this person, who was clearly expecting me somewhere else. I worried, that I had misunderstood, that it was my fault, but no, when I asked Peter Wrigley what I should do, he told me, in no uncertain terms, that I was supposed to be in his Out-patients, but he did kindly let me go to the Leukaemia Clinic.

There, with some trepidation, I see my first patient in follow-up of acute myeloblastic leukaemia (AML). After 10 minutes, I am called to the phone: an angry voice asks, 'Where are you? You're half an hour late. You're meant to be seeing the Outriders with me!'. Whilst I had been warned about the idiosyncrasies of this medieval institution, which apparently superseded even those of Guy's (my Medical School), this was something else altogether - visions of visored, black-leather-clad motorcyclists…who were these 'Outriders', and where were they to be found? I explain that I am already meant to be in two Clinics simultaneously and we negotiate to meet 'on the stairs' at 2 o'clock. Fine.

So I go straight from the Out-patients to a large, stone staircase in the King George V building, but Chris Gallagher (Consultant Physician in Medical Oncology) is not there. Twenty minutes later he appears: 'Where were you?' It transpires that there are two, identical, parallel staircases at either end of this confusing building. It also becomes apparent that the 'Outriders' are patients on 'outlying' wards. We have seen two people when Chris receives a phone call (for me); an angry voice, this time a woman's, asks, "Where are you? We've

been waiting for you for half an hour to come and do the Day Ward!' I run there, am taught how to give chemotherapy by the altogether amazing Carol Willock (a nurse on the Day Ward, and amazing cook, treating us all to wonderful meals at Christmas and leaving parties!) and at 7pm, miserable and hungry, wishing that I had never come to this strange place where people seemed only to shout at one another, I go back to the Department. There I encounter a smiling, charming Jim Malpas, who asks, 'Have you had a good day?'…….

It did get better. A year later, having completed my appointment at Hackney Hospital, and inspired by two talks I heard at the annual, Departmental Review Meeting of 1978: Mel Greaves's (now Director of the Centre for Evolution and Cancer, Institute of Cancer Research) account of his work on the biology of acute lymphoblastic leukaemia, and Andrew Lister's, in which he referred repeatedly to the possibility of *cure* for AML, I returned to Barts as a Research Fellow (funded by the Imperial Cancer Research Fund (I.C.R.F.), and stayed for the next 32 years. It gives me much pleasure to recount some of the adventures and successes (although there were also failures), of that time.

When asked, say, at a dinner party, 'What do you do?', the response to my explanation was often some expression of how depressing, distressing or both that must be. On the contrary, it was very exciting, when desperately ill people got better, against all the odds. And when they did not (which in 1979 was often), it was anger that I felt at our inability to change that. The feeling remains, although I now do other things. In retrospect, the best thing about working at Barts was this strong, common ambition of trying to improve therapy for people with haematological malignancy, the overriding aim being to develop curative treatment.

For me, this was first manifest in AML, new protocols being developed and new drugs being evaluated. Studies on the pharmacokinetics of cytosine arabinoside and other drugs were made possible through close collaboration between Maurice Slevin (later Consultant in Medical Oncology), at the time, like me, a Research Fellow, and Simon Joel (who remains 'Joss' to me; now Emeritus Reader in Experimental Cancer Medicine). Collaboration and this sense of shared purpose were fundamental to the way in which the Department worked. The extraordinary attention to detail of John Amess (Consultant in Haematology), Alfred Stansfeld, and later Andrew Norton and Maria Calaminici (Consultants in Histopathology), as well as that of Rodney Reznek (Emeritus Professor of Diagnostic Radiology) and Sarah Vinnecombe

(Consultant in Radiology), together with their willingness, often at the end of a long day, to sit down patiently and show me *why* the diagnosis or extent of disease were as they would later report it to be, made all the difference. This principle of sharing information (or indeed uncertainty) is best exemplified by the weekly meetings at which all newly diagnosed patients with haematological malignancy and those with recurrent disease were discussed. Later of course, these were to be formalised as Multidisciplinary Team (MDT) Meetings, but those at Barts preceded the national introduction of the MDT meeting by at least 30 years.

A further aspect of such collaboration was that with 'the lab', which was in fact several labs, those of John Habeshaw (now Senior Lecturer in Pathology) Mike Horton (Professor of Medicine at UCL before his untimely death), and later, Bryan Young (Emeritus Professor of Cancer Genomics). Blood, bone marrow and other tissues were collected assiduously, Andrew Lister presciently (and relentlessly), reminding people of the importance of the frozen tissue bank. In parallel with maintenance of an almost unique, clinical database, expertly managed by Jackie Lim and later, Maxine Cambal, Janet Matthews, Andy Wilson and the indomitable Finlay Macdougall, correlations could (and continue to) be made between molecular aspects of the illnesses and clinical outcome. The result has been seminal contributions to knowledge on the biology of leukaemia and lymphoma, as well as publications, and of course, MDs and PhDs.

My own work, apart from looking after patients and teaching students, began with an MD project, to study the potential role of interferons in leukaemia and lymphoma. At the time, the drug was a source of much hope and excitement. The project will remain memorable for two reasons: first, the lymphoblastoid interferon cost (the I.C.R.F.) £1 million - extraordinary that a trial drug should have to be paid for - and second, that despite the tremendously exciting (to me anyway) demonstration of highly significant *in vitro* activity against myeloid blast cells, the clinical correlate, a reduction in the number of circulating leukaemic cells, was not reflected in meaningful responses for patients with recurrent leukaemia. Sadly, the drug did not help anyone with AML, although for a while, it became the optimal treatment for Chronic Myeloid Leukaemia, (other than an allograft), prior to the advent of the tyrosine kinase inhibitors, which changed everything. Interferons were also used later with some success as adjuncts to chemotherapy and as maintenance therapy in Follicular Lymphoma. In collaboration with the memorable in every way, Derek Crowther, and later, John Radford, we contributed to those studies. I remember

many happy times in Manchester; the relationship with the Christie Hospital was very special and totally reciprocal.

Having written my MD thesis, I was appointed to the staff of Barts, on a specific I.C.R.F. grant, to establish high-dose treatment supported by autologous bone marrow 'transplantation' for leukaemia and lymphoma. I thank Walter Bodmer and Mike Crumpton (Director and Deputy Director of the I.C.R.F.) for their faith in me and for their subsequent friendly and good advice. The first year was to be spent at the Dana Farber Cancer Institute in Boston, a place where, to my surprise, having read their numerous clinical papers, floors and floors of cells and mice, nude or otherwise, far outnumbered those inhabited by people. Never having worked in a lab before, (not being a Haematologist), at first I found the techniques for *in vitro* depletion of morphologically undetectable tumour cells from autologous bone marrow quite difficult - I owe Lee Nadler (Professor of Cancer Research and Teaching, Harvard Medical School) and Jerry Ritz (Professor in Tumour Immunology, Harvard Medical School) special thanks for their patience with me and for their friendship.

On my return to Barts, with much excitement and some trepidation, we began treating patients with myeloablative therapy, and their bone marrow with monoclonal antibodies and complement. The latter was only made possible with the help of Mike Horton, Keith Adams, Lindsey Goff and Elaine Dorey. There followed an exciting time of developing the use of high-dose treatment for lymphoma, supported by autologous bone marrow (and subsequently, peripheral blood progenitor cells). Initially, the whole process - from collecting bone marrow from the patient under general anaesthetic in the morning, to the three cycles of 'treatment' of the mononuclear cell fraction with antibody and complement and then freezing the cells - took all day and a lot of the night. I remember going home on Tuesday evenings, briefly, to say goodnight to my small daughter, before returning to Barts.

For the person who was ill, the treatment, Gram doses of cyclophosphamide, followed by fractionated total body irradiation (TBI) was very difficult; there was an appreciable mortality and morbidity, including permanent infertility. I thank the patients who took part in these early studies; unquestionably we helped some of them, but by no means all. Nonetheless, as a consequence of the encouraging early experience in patients with recurrent B-cell lymphoma, we extrapolated to AML, initially in patients with recurrent disease, who were otherwise almost certainly incurable, and then, as consolidation of first

remission in newly diagnosed patients. The results in this second group especially, were very exciting, the proportion of younger patients cured increasing from approximately 25% with conventional therapy to 40%, there being no better results at the time. Thankfully, this highly toxic treatment has now been largely superseded, but I am writing about 25 - 30 years ago. It is hard to convey the excitement of being part of something new that really made a difference to outcome. These studies were conducted in collaboration with other British and European centres and led to subsequent work and close friendships with Renato Bassan and Tiziano Barbui in Bergamo and Magnus Björkholm in Stockholm.

I return to the most special thing about the Department, the sense of working with like-minded people, whose aim was always to be thinking in terms of developing curative treatment for haematological malignancy. To this end, we were in the forefront of the investigation of new cytotoxic therapies such as fludarabine and velcade (bortezomib) and entirely new treatment modalities for lymphoma, such as monoclonal antibodies, (originally proposed by Ehrlich) and now a component of standard treatment for B-cell malignancies and, concurrently, the evaluation of radio-labeled antibodies. It was an exciting time. The development of 'HAART' (for treatment of patients with HIV/AIDS), apart from stopping people with this diagnosis from dying, meant that we were able to treat lymphoma successfully, which not infrequently develops in such patients. My colleague, Silvia Montoto, in collaboration with physicians from the Department of Infection and Immunity at Barts, continues to lead this effort, which resulted in the setting up of a joint clinic.

No-one works in isolation. The other, very special thing about Barts was that when you needed help, it was always forthcoming, in the form of marvelous, immensely knowledgeable people for whom nothing was too much trouble. They didn't send a Registrar, they just came; for surgery, William Shand and John Chalstrey; from Radiotherapy, Arthur Jones and Sid Arnott, Sid memorably trying to reassure me when we first used total body irradiation (TBI) as part of high-dose treatment at Barts. Similar, unequivocal help and support was provided by Seamus Banim (Cardiology), Larry Baker (Radiology), Jeff Gawler (Neurology), Ruth Seifert (Psychological Medicine), Charles Hinds and Dave Watson (Intensive Care), John Moore-Gillon (Respiratory Medicine), Mike Besser and then John Monson (Endocrinology), in that and every possible order.

Of course I have been selective, memories are, but I should not omit my frustration at the repetitious nature of a sequence of NHS evaluations such as the Tomlinson report. On a personal note though, they gave me the opportunity to meet Bob Park, the 'human face' of the Administration. Subsequently, in the light of the junior doctors' working time directive, I am very glad that no-one ever told me when to go home.

An important part of my life at Barts was teaching medical students. I am lucky to have worked in a Medical School, which thanks largely to the enlightened views of Lesley Rees as Dean, embraced the concept of an integrated undergraduate course, as pioneered at the University of Maastricht and McMaster University. Much criticised by the traditionalists of British medical education, the notion of teaching Anatomy, Physiology, Biochemistry and Pharmacology as they relate to the reality of an illness, from day 1, and introducing 1st year medical students to a person with that illness, has to be a better way of learning than considering these disciplines as purely theoretical concepts. Furthermore, introduction of the 'Graduate entry' course in Medicine, enabled people with a background of excellence in other fields to join and enhance the student body by their previous experience. Encouraging students from ethnic minorities to apply was also something 'close to my heart' and commensurate with the needs of the local population that Barts now serves.

Just as Peter Wrigley, Tim Oliver (Emeritus Professor of Oncology, Jim Malpas and Andrew Lister 'imparted their art' (Hippocratic oath) to me, the training of doctors wishing to pursue Medical Oncology or Haematology as a career was an integral part of our work at Barts. These people later continued the Barts tradition by becoming the academic staff of Oncology and Haematology Units in the UK and throughout the world. Notably, Trivadi Ganesen, 'Ganesh' (like the god), having worked in Oxford for many years is now Professor of Medical Oncology at the Cancer Institute (WIA) in Chennai, Mike Barnett went to Vancouver to run Leukaemia and Bone Marrow Transplantation in British Columbia, 'Dhali' Dhaliwal to Thunder Bay, as director of the Cancer Centre there, Amit Oza, to the Princess Margaret Hospital, Toronto as head of Gynaecological Oncology and Mark Doreen to Halifax, Canada, as Head of Medical Oncology. Bruce Ponder became Director of the CRUK Cambridge Institute, Jonathan Shamash and Sarah Slater, consultants in Medical Oncology at Barts, as did my Research Fellow colleagues, Chris Gallagher and Maurice Slevin. Others 'defected', Mike Richards joining the higher echelons of government, and Peter Johnson those of Cancer Research UK, Peter concurrently being head of the Oncology Unit in Southampton where he was

joined by Andy Davies (Senior Lecturer and Honorary Consultant in Medical Oncology), The list of consultant appointments continues: Rajnish Gupta in Limerick, Jonathan Waxman at the Hammersmith, Jeremy Whelan and Sandra Strauss at University College Hospital, Mark Bower at Chelsea and Westminster, Peter Clark in Liverpool, Kim Last in Sheffield and Carol Davis in Southampton. We were also lucky enough to work with doctors from other countries, who have remained close friends: Lukas Dadiotis, John Apostolidis, Vassiliki Pappa and Anna Pigaditou from Athens.

I must also mention the very special nursing staff, notably, Yvonne Terry (who in 1979, taught me to work cell separators, something that as a Registrar, I was apparently not supposed to do), Nancy Hallett, later to become Chief Executive of Homerton Hospital, as well as Claire Murrell (Lead Cancer Research Nurse at Barts Cancer Institute), Ruth Bradley (Director of Care Services, St Joseph's Hospice) and Elaine Stewart (Cancer Support Specialist at Maggie's).

As Jeff Gawler recently said, these were halcyon days but there was also opportunity for dissent. A highlight of the week, when I was a Research Fellow, was the weekly 'Revolution'. After a particularly difficult week - I cannot now even remember what the problem was - a group of us, disaffected and angry, wanted to air our grievances to Andrew Lister. What started as 'revolution' rapidly became a tradition, actually no, an 'institution'. Grievances aside, the 'Revolution' was the time in the week when Registrars in the hospital met Research Fellows working in the lab; the senior nurses sometimes came, work in progress was discussed, presentations were rehearsed (by consultants, research fellows and registrars alike), and all of this, to the accompaniment of very good wine. Often, when eminent visitors from abroad were invited to give a talk, which they might be giving in London the next day, they nonetheless first had to sit through the business side of the Revolution.

It remains for me to say thank you, first, to Maurice Slevin for his friendship and encouragement always, when we both worked as Registrars in Medical Oncology at Hackney Hospital, and to all my colleagues at Barts who made it possible for me to work for the International Network for Cancer Treatment and Research (I.N.C.T.R.), for half my time, over a 5-year period. As director of the London branch of a 'not-for-profit' organisation founded by Ian Magrath, to help people with cancer in developing countries, my remit was Education and Research. The former involved teaching doctors and nurses in places as disparate as Pakistan, India, Nigeria, Tanzania, Egypt, Turkey, Brazil and

China. The teaching itself encompassed many different things: from discussion of new treatments and how best they might be adapted to local needs and possibilities, to encouraging and teaching doctors-in-training how to write abstracts and manuscripts for publication, and in China, trying to convey the importance of the concept of 'informed consent' for patients taking part in clinical trials.

The other aspect of my job was, with Ian Magrath and Melissa Adde, the setting up of and then running, a collaborative clinical trial in patients with African Burkitt Lymphoma. The remarkable thing was first, that this happened at all, with haematologists at four University Hospitals in Nigeria, Tanzania and Kenya, none of whom had ever previously worked to a common protocol, working together and with us. The second extraordinary thing was the quality of the data collected - as the study monitor, I checked the data against the notes, as you do. And best of all, despite the numerous difficulties inherent in working in these countries, the greatest of which is often, very late presentation, parents sometimes carrying their dying child for days and many miles to get help, now, more than 600 patients have been treated, and the cure rate is 40%. The results were presented at the Lymphoma meeting in Lugano by Muheez Durosinmi (Professor of Haematology, at the University of Ile-Ife, Nigeria) to much acclaim and respect, and subsequently published in the *British Journal of Haematology*. For my part, I learnt a great deal and really appreciate how lucky we are to live in a country with a National Health Service.

I return now to that fateful first day: my thanks to Peter Wrigley for teaching me the fundamentals of Cancer Medicine before I started at Barts, to Chris Gallagher (the second angry voice on the phone), who lent us his wards for more than 6 months when the floors in the Bodley Scott Unit started to disintegrate, to Jim Malpas, for teaching me about myeloma, and for wisdom and good advice, always, and to Andrew Lister (the first angry voice), who taught me everything I know about the management of people with leukaemia and lymphoma. I feel very privileged to have worked at Barts.

A Ward Sister's View

Jenny Ellwood
Former Ward Sister, Gordon Hamilton Fairley Unit,
Hackney and Homerton Hospitals

In the June-July 1976 issue of 'Daylight', the Barts Hospital news magazine, there is an account of the opening of the newly renovated cancer wards at Hackney Hospital by Princess Alexandra and her husband Angus Ogilvy. The article in the Magazine is entitled "A Lasting Memorial" and is attributed to the late Professor Gordon Hamilton-Fairley who was assassinated by the IRA in 1975.

I understand it was his vision to have a cancer service for the residents of East London as he was given £6000 donated by the Dawn Trust to set up this Unit by relatives of one of his patients at Barts. Sadly, he did not live to see his vision fulfilled. With other monies from the Imperial Cancer Research Fund and the Regional Health Authority, a 30-bedded Nightingale Ward in the B block of the old Victorian Hackney Hospital was converted into two wards of twelve beds each. It was very new and smart and in those days became known as the "Hackney Hilton". One ward was named after Sir Ronald Bodley-Scott and the other Gordon Hamilton Fairley. In later years the Unit became known as GHF after its founder.

"A Lasting Memorial" concludes "…that it is hoped these new facilities will not only provide a lasting memorial to the late Professor Hamilton Fairley, whose vision and great energy contributed so much to the creation of the new Unit, but will also enable significant advances to be made in the treatment of malignant disease."

In 1977, I was appointed by Dr Peter Wrigley to be the ward sister of this Cancer Unit. It had been during my experience as a surgical ward sister that I became aware of chemotherapeutic agents being given to patients with abdominal tumours, and we as nurses were given little guidance to the symptoms produced by these techniques. I wondered why are the wounds not healing? I wanted to find out. I saw an advert in the Nursing Times for a Ward Sister at

the new Cancer Unit at Hackney Hospital, a joint initiative with Barts. I applied and was appointed by Dr Peter Wrigley. In those early days, cancer nursing was in its infancy and I had to learn very quickly. I attended courses at the Christie Hospital in Manchester and the Royal Marsden in London. My colleagues at Barts were very supportive, especially Sister Yvonne Terry and Dr Ama Rohatiner, who came to Hackney as my first Registrar. Those first few months at Hackney were very difficult. We had few permanent nursing staff and mostly agency nurses, who were frightened of people dying, which they did. It seemed to me that patients were referred too late in their illness and were too ill for chemotherapy. Most of these patients had lung cancer. Hackney and Glasgow were the two areas in the country where the prevalence of lung disease was due to cancer. Both cities were industrial and near the docks. The patients who were referred were elderly and had frequent chest infections.

It was in 1979 that Dr Maurice Slevin from South Africa joined us as a Registrar. He had new ideas about the criteria for admission for treatment and gradually newly-diagnosed patients were admitted and did respond to treatment. The pathology of tumours of the lung was either oat cell or squamous cell carcinoma. The treatment of choice for oat cell tumours was a drug called Etoposide, known as VP16-213. The treatment for squamous cell tumours was, and is, radiotherapy.

A small laboratory had been established away from the ward and I recall it had one Bunsen burner and one research assistant, Simon Joel, now Dr Joel, known affectionately as "Jos". One person, who was with us from 1977, was Mrs Renee Smith with the grand title of Housekeeper. She was responsible for the kitchen, ordering of food and supplies and keeping everyone in order. She was a real character with a Cockney sense of humour. One day when Peter Wrigley was teaching medical students what to look for on a chest x-ray, she handed him his afternoon tea and smartly replied, pointing to the white area on the x-ray " that's it, that's the tumour!"

About this time, the School of Nursing at Barts arranged for third-year student nurses to work on the ward – this was wonderful. They were highly motivated and professional and enjoyed the challenge of working in the now, popular Unit. From student nurse status, I was able to employ staff nurses and thence sisters of the future. With the support of the School of Nursing, we were able to produce a teaching programme for them.

Myself with staff at the old Hackney hospital, Christmas 1980

About this time, the School of Nursing at Barts arranged for third-year student nurses to work on the ward – this was wonderful. They were highly motivated and professional and enjoyed the challenge of working in the now, popular Unit. From student nurse status, I was able to employ staff nurses and thence sisters of the future. With the support of the School of Nursing, we were able to produce a teaching programme for them.

I have a note from 1982 from Dr Maurice Slevin asking my opinion of a job description he had compiled for two day-care Oncology nurses to work a thirty seven and a half hour week on the Unit. This was an innovative idea because Oncology or cancer nursing as a specialty was in its infancy. It was not until September 1985 that the City and Hackney Health Authority funded an English National Board course for trained nurses. These two nurses would organise the care of day patients with the Consultant and Senior Registrar. They would obtain results of blood tests, x-rays and scans etc. and would assist with giving the chemotherapy and so would lessen the patient's time as in-patients. Dr Slevin stated that in the future it would be envisaged that their work would include administration of cytotoxic chemotherapy, this is taken for granted now.

We now had our own teaching programme on the ward, assisted by a clinical nurse tutor from Barts. This covered the side-effects of chemotherapy due to the toxicity of the treatment, especially skin care and oral hygiene which were important. Every patient had a mouth care tray at their bedside. Nutrition was

high on the list and the effects of poor appetite and weight loss were identified. Mrs Smith, our Housekeeper, was acclaimed for her breakfast porridge which she made and served herself. I remember we were also allowed extra nourishment, like eggs and milk, from the supply kitchen. Much to the consternation of the domestic staff, we bought individual teapots for every patient for teatimes to try to increase the patients' fluid intake. A glass of sherry was prescribed and served before meals in an attempt to increase patients' appetite. This was ordered from the Pharmacy and came up in medicine bottles!

We now had a variety of people working on the ward, Day Care Nurses, a Social Worker, Ancillary Nurses and Medical Students. Patients and their families were questioning their diagnoses, treatments and the prognosis. I felt they needed more time to discuss their feelings. At that time, the Hospital Chaplain was elderly and near retirement. With the agreement of the team, I ventured to ask the Sisters of the Community of St. John the Divine if they could help with some pastoral visits. I was and still am an Associate of this Community. They had a house in Bow where they moved from Poplar. The Community was depicted in the BBC TV series 'Call the Midwife'. Sister Iona came willingly on a weekly basis and was dearly loved by us all, patients and staff. She was free to spend valuable time with people who just wanted to chat and express theirs fears. She was a great asset. Sometime later the Rev. Douglas Hiza was appointed Anglican Chaplain to Hackney Hospital. He was a young energetic priest, a bereavement counsellor and psychotherapist. It became apparent there was never enough time during the day or at clinics to really have time to listen to our patients and their relatives. So as a team, we decided to form a Patient Support Group.

One of our staff had been to Gartnavel Hospital in Glasgow, where the first Patient Support Group had started. It was known as Tak Tent ('Take Care' in Gaelic). Those first pilot meetings were like treading on egg shells. Should we put patients, relatives and bereaved families together or separately? How would we cope with difficult and angry reactions? We met in the Nurses' Home sitting room and provided refreshments, but decided against sherry. The first meeting was held on the 7th September 1983, with just ten invited patients and their families. We decided on a ratio of three patients to one member of staff. It went well. The Support Group flourished and met regularly on a monthly basis, ably supported by Jane Hartwright who dealt with all the administration, much to my relief!

We produced a Patient Information booklet with details of travelling directions, location of the Unit in the hospital, details of the members of staff and colours of their uniform, daily ward routines and open visiting times. The Support Group continued for the next ten years. One couple who attended our Support Group were Maureen and Harry Bernstein. The Bernsteins belonged to an amateur dramatic group and asked their friends to put on a show to raise funds for the Unit. It was a musical called 'Encore' and was held in a Community Hall in Hampstead in September 1984. The funds that they raised for our Unit were used to purchase the little extras for our patients such as nice pillows, heat pads and comfortable chairs for the patients having treatments as day patient were sitting for several hours.

The setting up and evaluation of a hospital Patient Support Group was the first subject for nursing research. Buckman wrote in 1980 'the art of good communication is essential at all levels of those associated with a potentially life threatening disease, such as cancer. Patients are often left to their own devices in dealing with their feelings often as a result of the professionals' own discomforts and inadequacies in that area'. Our Support Group was perceived as being an extension of the great camaraderie which developed between the patients, their families and many of the staff. This was due I think because we saw them regularly every three or four weeks over the course of their six month treatment. As well as a Patient Support Group, it was decided we would all benefit from a staff support group. It was held on a weekly basis at lunch time with sandwiches provided and was facilitated by Dr. Ruth Siefert, a consultant psychiatrist. All grades of staff were invited to attend and all manner of topics were discussed and feelings expressed and it was sometimes very heated.

As an example of subjects discussed, asbestosis and industrial diseases had particular relevance in East London due to the types of industry prevalent in the area of the Docks. Mrs Nancy Tait's husband had been a victim of mesothelioma and the family had not received any compensation for what was, essentially, a work-related disease. Mrs Tait campaigned for the victims of industrial diseases to be legally entitled to compensation from their employer. She was awarded an MBE in 1996 for her work, having established and let the victim support group, the Society for the Prevention of Asbestosis and Industrial Diseases now known as OEDA (Occupational and Environmental Diseases Association), which lobbied for tighter asbestos controls. Nancy met with formidable opposition, but was proven right - low-level exposure causes mesothelioma, white asbestos (chrysotile) is not "safe", and asbestos dust causes lung cancer in the absence of asbestosis.

One very special patient in the Patient Support Group was Vicky Clement-Jones, who was a doctor herself. She attended with her husband and contributed to the discussions so eloquently. One thing that bothered the female patients was the loss of hair and the distress of hair falling everywhere in clothing and food. Vicky devised the use of a hair net and the now well-known head scarf. It was through these support meetings she had the vision of founding a patient information service. Her Charity became BACUP, the British Association for Cancer United Patients.

To raise funds for her charity, from her hospital bed, she would write to various charities, bankers, lawyers and financial groups in the City for financial support enabling her charity to become formalised. She was very frustrated by all the bureaucracy this entailed but she persevered, realising that time was not on her side, as she now had advanced abdominal malignancies.

Fun Run in Hyde Park c.1980 in aid of BACUP, picture includes Maurice Slevin, Kevin O'Sullivan, Fred Horne, Mary Horne, Vicky Clement-Jones and Hackney & Homerton patients

It was early in 1987, she was invited to appear on the early evening BBC television Terry Wogan chat show. She was determined to go to talk about her charity. I was privileged to accompany her to the show by taxi to Shepherds Bush in the evening rush hour from Hackney – it was a long drive. Her pain was being managed with diamorphine administered via a syringe driver. She managed the

It was early in 1987, she was invited to appear on the early evening BBC television Terry Wogan chat show. She was determined to go to talk about her charity. I was privileged to accompany her to the show by taxi to Shepherds

Bush in the evening rush hour from Hackney – it was a long drive. Her pain was being managed with diamorphine administered via a syringe driver. She managed the interview successfully, but collapsed exhausted afterwards before making the return journey to Homerton. That experience had an amazing effect on people tolerating this disease. Correspondence flooded in and a friend became her PA and assisted with her vision to get the charity up and running.

The play 'Shadowlands' was being performed in Shaftsbury Avenue which depicted Nigel Hawthorn as C. S. Lewis who had cared for his wife, Joy, with cancer. All the actors and the theatre management donated their time for the benefit of BACUP. It was a memorable performance.

Sadly, Vicky died in August 1987. We all her attended her funeral service and later Reverend Doug Hiza preached at the Service of Thanksgiving for her life in St. Paul's Cathedral. It was packed with relatives from Hong Kong, colleagues from Cambridge and Barts and many friends from Hackney. BACUP became a flourishing telephone information service and published many booklets on the various cancers and their treatments. It is now part of the McMillan Support Service.

In the summer of 1986, we moved to the newly built Homerton Hospital across the main road from Hackney. It was a modern building on two floors with landscaped grounds and individual courtyards between the ground floor wards. We were all delighted with the new building. The nurses and doctors had their own office space and there were changing rooms for staff. The Secretary's office also housed nursing and scientific journals and acted as a small library for the staff.

Over the years, we had many research nurses collating nursing research in the following areas: oral care, taste changes, cancer cachexia, comparison of energy supplements like Polycal and Duocal, depression and the use of anti-depressants, relaxation methods, the Hickman catheter, quality of life and fighting spirit- its prognostic significance, setting up an evaluation of a Patients Support Group all for patients receiving chemotherapy. Dietetic students from the University of Surrey came to us to study nutrition in cancer patients

receiving chemotherapy. One of those delightful students was Susan Parkinson who is now Susan Jebb, Professor of Diet and Population Health at Oxford University. She is frequently on the BBC talking on the problem of obesity in Britain. The results of the nurses' research was printed in nursing journals.

Staff Picnic, 1986, at the new Gordon Hamilton Fairley ward. Includes Sister Angela, Richard Osborne, Kevin O'Sullivan

As nurses, we were encouraged to keep abreast of the latest nursing practices and research from all parts of the world. In 1988, a fifth International Cancer Nursing Conference was held at the Royal Festival Hall on the South Bank. It was arranged in association with the Royal Marsden Hospital and was a week-long series of meetings and events. Nurses came from all over the world and gave presentations of their work and their research. I had had the honour of representing our Unit at the first International Conference on Cancer Nursing in Melbourne, Australia. These were great opportunities to meet colleagues who were encountering the same problems with the disease of cancer, its treatments and associated psychological problems.

In January 1987, the new Homerton Hospital was officially declared open by the then Archbishop of Canterbury, Dr. Robert Runcie. He spent the whole day in the Hackney area visiting various departments including the Psychiatric and Geriatric units. In the afternoon, a Service of Thanksgiving was arranged in the staff restaurant. The service was organised by the Anglican, Catholic and non-

conformist Chaplains. The choir was made up of people from different departments in the hospital. The service was packed with patients in beds and chairs, their relatives, staff and distinguished guests from the community. Dr. Runcie dedicated the little chapel, which had been the chaplain's office, to the memory of a former Anglican Chaplain in Hackney, Father Hooper.

The Archbishop of Canterbury pictured with Vicky Clement Jones and myself

The Archbishop's itinerary included a half hour visit to a ward before meeting the official delegation for afternoon tea. The ward chosen was our Gordon Hamilton Fairley Oncology Unit. Dr Runcie decided to stay for one and a half hours and so missed his official tea! I had the privilege of conducting him around the ward and introducing him to all the patients.

In one of the side rooms, an elderly Muslim gentleman raised his hands in prayer and said "Allah be praised" to which the Archbishop replied "Indeed; Allah be praised". One of our lovely West Indian mums had made a large, decorated fruit cake and this was ceremoniously cut by the Archbishop amongst much delighted approval. I have a lovely photograph of the Archbishop with Vicky Clement-Jones (see above) with whom he chatted for some time and myself. It was a memorable occasion enjoyed by all. Later, I wrote to Dr. Runcie to thank him for his pastoral visit and in his reply he sent a photograph of himself in his Archbishop's cope and mitre to be hung in the ward.

I continued to manage the day to day running of the ward, helped by Sister

Christine Panton, with Sister Theresa Coyn and Sister Cecile Messent on night duty. It was a happy team. Chris Panton came to Hackney in 1981 and, between us, we developed various teaching programmes, objectives and philosophy of care for students and staff nurses. This included details of treatments offered, their terminology and the nursing care needed for those treatments. The protocols for treatments were carefully documented by Dr. Paul Revell, Senior House Officer and now Consultant Oncologist in Stafford. As a team, we assisted in the teaching programmes for the Stoma Nurse course for students at Barts, the final year nursing students at the London and the nurses from St. Joseph's Hospice, who required knowledge of chemotherapy treatments and their after-effects. Eventually, the English National Board course commenced at Homerton, with a nurse-tutor from Barts.

Over the years, I have met some very remarkable patients and their families who became our friends. They were admitted every three or four weeks for treatment so we got to know them very well.

I have mentioned earlier that the Oncology Unit was at the Hackney Hospital. The Victorians had built wide verandas outside the wards which overlooked the grounds and which had access to the fire escape. We managed to supply some seating for the patients and some window boxes. There was no Occupational Therapy in those days. One autumn afternoon, we bought some daffodil bulbs and those patients who were able helped to plant them. One of those patients was a young man named Alan. He knew he had a cancer, but in my notes of that time he expressed concern for his Mum and was concerned that she would be alright when he was gone. I tried to reassure him and then he said "These daffodils will bloom next spring and I shall never see them but you will Sister. Will you remember me then"? I remember him in springtime every year.

Bob Cole was another very brave patient. He was diagnosed with myeloma and was the first patient of ours to undergo a bone marrow transplant. This meant being isolated in a very small side room and nursed with strict aseptic techniques to avoid cross-infection. It was very boring to be enclosed in such a confined area day and night, with no visitors being allowed in the room, and only the same staff being allowed to care for him, with the ritual undertaking of wearing special gowns, masks and gloves. He survived and I hear from his wife every Christmas.

The opening of the Daffy Duck day room extension in May 1992. Pictured are Daphne Hamilton Fairley, Peter Wrigley, Mary Horne and Derek Hack

Fred Horne was another character. He was a local man with a real colonel chin-strap moustache. Whilst receiving treatment as a day patient, his wife Mary would contribute tea and coffee and serve it in the day room to the other patients. This continued long after his course of treatment, so much so that he started fund-raising for the unit, not only for refreshments, but also a mini-bus to take patients up to Barts for their radiotherapy and scans. Transport to Barts was tiring for patients, as they had to be taken by ambulance for a half hour radiotherapy treatment, and then had to wait for hours to be transported back. It also meant the ward lost a nurse for the day due to transport duties. Through Fred's enterprise, the money was raised, the mini-bus bought and Fred became the driver. The League of Friends of the Homerton assisted financially and the Daffy Duck Fund was born! Everyone was given a small yellow plastic duck and T-shirts were sold to raise funds. This fund also bought fans for patients in the summer months, heat pads, clocks for the wards and side rooms, and petty cash to get patients home by taxi from hospital. Garden plants were bought for the enclosed gardens.

The biggest project that Fred and Mary worked on was raising funds to build an extension of a dayroom with kitchen facilities for patients and families. The original dayroom had been taken over for day patient treatments, ward meetings, x-ray meetings, ward rounds and the weekly staff support group. In September 1989, Fred and Mary, with the League of Friends, arranged a fund-raising evening of fun and entertainment and a five course meal at the Talk of The Town in central London. The programme was entitled 'An Evening to Remember' and it was indeed. Those of us off duty attended and had a happy evening. Thousands of pounds were raised through tickets and advertisements in the programme and plans for the new dayroom commenced. At that time, a BBC programme called 'Hearts of Gold' hosted by Esther Rantzen was in vogue. Fred was nominated for an award in recognition of his community spirit and dedication to the welfare of our patients.

Early in 1992, Dr Wrigley introduced Mrs Norah Reed, who had recently been bereaved, to the Support Group. Her husband, Barry, had been treated by Dr Wrigley. She offered help as it had been suggested the Cancer Laboratory at Homerton needed funds for cancer research and she had the essential business skills to help raise money. She took no time in getting started by having a leaflet published, outlining the aims of the laboratory, which was to be called The Barry Reed Medical Oncology Research Laboratory, in memory of her husband. The work of the laboratory would focus on research into new drugs to be used in the treatment of cancer, their benefits and their side-effects. This was the beginning of a lasting friendship with Norah.

Jane Hartwright and Norah Reed in 1997

One of the first major events Norah organised to raise funds for the laboratory was 'An Evening with Dirk Bogarde' (pictured) at the Theatre Royal in the Haymarket in June 1992. He donated his time and talent with readings from his books and other famous authors. The books were on sale, a champagne reception was held in the Circle Bar and the magnificent sum of £25,000 was raised for the lab. The fund-raising has continued over 23 years and includes the annual Gala Dinners at Christmas and the Summer Concerts with entertainment in the Great Hall at Barts. Norah has, since 1992, worked tirelessly to get over £1,000,000 for the work of the Laboratory. This money has provided much-needed expensive equipment for laboratory use and this year, 2015, has extended into the provision of three-year funding for three PhD research students to work on cancer related research projects.

A political storm was looming. St. Bartholomew's Hospital was doomed to closure and there were many protests. The result was that Barts lost its A&E Department, but the wards were kept open. These changes meant that the Oncology Unit at Homerton had to move to an old Nightingale ward at Barts. There were many protests and our secretary, Pat Jacobsen, was inundated with letters. The complaints were mainly about its being further for patients and families to travel, the lack of parking places at Smithfield and the second floor ward having little access to the gardens. Many felt this was a retrograde step.

Nevertheless, in December 1992, despite the many protests, the Pickford vans arrived in their dozens to transfer furniture, filing cabinets and laboratory equipment to Barts. It was a sad time for us all as not all the nursing staff were transferring. The future of the Support group was also in jeopardy because not all the staff would be working at Barts. Therefore, it was considered impractical for the group to continue. It was the end of an era.

In conclusion, I think of the legacy of Gordon Hamilton Fairley's 'Lasting Memorial'. I remember Professor Malpas once saying he was so proud of 'all his boys" whom he had taught and who are now leading the way in Medical oncology all over the world. Also that essential research continues in the quest

to find answers to the treatment of this disease. Nurses, too, are now consultants in the field of nursing, throughout the country, sharing their enthusiasm for good quality nursing care and advising the government on policy-making.

I remember, with gratitude, the many colleagues I have worked with who were so supportive over the years, but most of all I am indebted to the patients and their families who bore their illness with such fortitude and grace. Some I have mentioned, but there were many, many others over the years. I feel very privileged to have been part of this special story.

Cancer Pharmacology

Simon Joel
Emeritus Reader, Experimental Cancer Medicine

Let me first set the scene. The Cancer Pharmacology Group at Barts was founded in the summer of 1982 with the appointment of Maurice Slevin as Consultant Physician, Maurice had trained in South Africa before completing his MD at Barts, studying the clinical pharmacology of cytosine arabinoside. He soon assembled a research team to investigate the effect of schedule on the activity of etoposide in small cell lung cancer, with Vernon Harvey as the clinical research fellow and myself as the analyst to assay the hundreds of pharmacokinetic samples that resulted.

As a new research group, the only equipment we possessed were two deep freezers for storing research samples. Our lab space at the then Hackney Hospital, where patients with solid tumours were treated, was being used temporarily by Pathology, so for some time we were accommodated by the Clinical Pharmacology Department at Barts, which was led at that time by Professor Paul Turner, a distinguished pharmacologist and founding editor of both the *British Journal of Clinical Pharmacology* and *Human Toxicology*. Professor Turner was always very supportive of our research, while in the lab we were very ably guided by one of his post-docs, Atholl Johnston, now Professor of Clinical Pharmacology at Barts, who was, and has continued to be, a friend and valuable source of advice on all things analytical and drug pharmacokinetics.

For the first six months, Vernon and I were closeted in a small room in the department, learning the hard way which parts of a high performance liquid chromatography (HPLC) system did what and then developing an assay for determining etoposide concentration in body fluids. Once that was done, we moved into our own lab space at Hackney, where we started to work our way through the 1,500 or so plasma samples requiring analysis. Unlike modern HPLC systems that automatically calculate the concentration of compound in patient samples, in the early 1980s, we had to adopt the rather more basic method of a plastic ruler and pencil!

Vernon and I were very ably assisted in this analysis by a large number of research students who came to work with us during their BSc placement year.

At the same time, Maurice appointed a team of research nurses to investigate psychosocial aspects of cancer, including a research nutritional student who developed ways of improving the diet of patients, using a range of supplements often incorporated into cakes or biscuits that were very willingly put through "preclinical testing" by the pharmacology lab team!

A common theme in our pharmacology research studies was in trying to improve the way that established drugs were used in cancer treatment by optimising factors such as the dose of drug used, the route of administration, or the duration of each treatment (also called the drug schedule), as Maurice had done successfully in his MD studies on cytosine arabinoside. The value of our work is best illustrated with etoposide.

One of the first studies that Maurice set up with Vernon in the early 1980s was a randomised trial to investigate the effect of schedule on the activity of etoposide, at that time an established drug in the treatment of small cell lung cancer (SCLC) and several other solid tumours. Published data suggested that this drug was best administered over several days, though in some trials the route of administration also differed between treatment arms (either intravenous or oral), so the data were not clear cut.

In this first study, small cell lung cancer (SCLC) patients were randomised to receive the same total dose of etoposide intravenously, but either in one go, as a single infusion of 24 hrs, or in 5 daily doses of 2hr infusions each. An important component of this trial was that all patients had blood samples collected repeatedly throughout treatment to enable blood levels of drug (pharmacokinetics) to be measured and related to the drug effects seen in patients. This study closed early, as after just 39 patients had been treated, it was already apparent that one arm was superior, with a 39% overall response rate in the 5-day arm compared with just 10% in the 24-hr arm, while bone marrow toxicity similar in both. The pharmacokinetic data indicated that the anti-tumour activity of etoposide was related to the duration of exposure to low blood levels, and so this was further investigated by conducting a second randomised trial, run by a new Clinical Research Fellow, Peter Clark, now Professor and Consultant Medical Oncologist at Clatterbridge Cancer Centre, Merseyside.

In this second study, we evaluated the same dose of intravenous etoposide administered over either 5 or 8 days. The 5-day and 8-day regimens had

equivalent activity in patients with SCLC, but, as in the first study, antitumor activity was associated with lower levels of etoposide, which resulted in less haematological toxicity. We, therefore, considered that prolonged exposure to low concentrations of etoposide may improve the therapeutic ratio for this drug, and that that low-dose oral etoposide might be regarded as a new therapy and evaluated as such. However, prolonging dosing, from 5 days to 15 days, was discounted for SCLC because, as with our first scheduling study, this trial also closed early, as after just 29 patients, there was already a clear difference in drug activity, with an overall response rate of 58% with 5-day etoposide compared with only 14% with the 15-day regimen. However, other studies showed the potential of prolonged infusional etoposide in ovarian cancer and in breast cancer. We also showed that oral etoposide dosing was unreliable because absorption varied according to the dose of drug used, mainly due to the poor solubility of the drug in the stomach.

The wealth of data that we had accumulated in these scheduling studies allowed us to identify relationships between blood levels of etoposide and both toxicity and anti-tumour activity, and how these were affected by changes in organ function. This research changed and informed the way in which etoposide is used clinically. Indeed, the importance of this work was highlighted in a special edition of the *Journal of Clinical Oncology* featuring Classic Papers in which two of our etoposide papers were republished (*J Clin Oncol*. Vol 4, No 1 1999: pp 119-128 and pp 129-139).

Shortly after establishing the lab at Hackney Hospital a second research fellow, Richard Osborne, was appointed to investigate morphine metabolism and its effect on tolerance. The starting hypothesis for these studies was that a morphine metabolite may accumulate with prolonged morphine use and may diminish its analgesic effects in the treatment of cancer-related pain. The first requirement of such a study is a sensitive, specific assay for determining morphine and its metabolites in body fluids. Nowadays, the method of choice for such an assay would almost certainly involve mass spectrometry. This was not widely available to research groups in the early 1980s, so we established an assay using HPLC. This had been reported previously for the quantitation of morphine, but we wanted greater sensitivity for our studies and to be able to also quantitate morphine metabolites, so instead of using the reported ultraviolet detection, we instead used the newer method of electrochemical detection. This was when the pain really started for us analysts! This method of detection was, and still is, notoriously sensitive to changes in temperature, electrical 'noise' and many other technical and environmental sources of

variation.

Using our newly-established assay, we demonstrated definitively, for the first time, that a metabolite of morphine, morphine-6-glucuronide (M6G), was present in the blood of healthy volunteers who had received morphine, and that this accumulated in patients with renal impairment. This observation initially came from measuring morphine and metabolite levels in patients with renal failure still requiring ventilation some days after receiving morphine and other studies by Richard Osborne, working with the Department of Anaesthesia at Barts.

The next critical step in these studies was to determine the effects of M6G in man. Before we could undertake such a study, we needed to establish that it was safe to do so. In this we were guided by Professors Turner and Dayan from the Department of Clinical Pharmacology and MRC Toxicology Unit at Barts, respectively. Based on results of pre-clinical testing of M6G, a single-dose study in humans was considered appropriate. Approval from the local ethics committee and national regulatory body was sought and received, and we proceeded to examine the safety, efficacy and pharmacokinetics of intravenous M6G in cancer patients with pain.

This was a 'first in man' study, which is always exciting, but to take a compound from synthesis and pre-clinical evaluation into our own 'first in man' trial added an additional frisson of excitement.

Intravenous M6G was well tolerated and, importantly, seventeen of nineteen assessable patients experienced relief of their pain after M6G treatment, with complete pain relief in seven patients. The onset of analgesia was rapid and consistent, with all but one of the responding patients reporting improvement in symptoms within 15 minutes of commencing treatment. The two patients in whom pain relief was not observed subsequently responded to treatment with pethidine. Despite its open, uncontrolled design, this study clearly indicated that M6G possessed significant analgesic activity in man with limited toxicity. Importantly, this direct demonstration of the pharmacologic effect of M6G strengthened our previous suggestion that the prolonged narcosis observed after morphine treatment in renal failure was due to accumulated M6G. Analysis of blood levels of M6G after M6G administration in this phase I study showed a strong correlation with renal function, confirming the importance of this route for excretion of M6G after morphine treatment, as suggested by our

earlier studies in patients with renal failure.

We subsequently carried out more classical pharmacology studies which helped us better understand the toxicity of M6G compared with morphine, studies that were conducted by Paul Thompson, a newly arrived research fellow from New Zealand, and a very talented research assistant, Naina Patel. Armed with these results, the logical next step was a head-to-head comparison of morphine and M6G, though this was difficult to undertake in cancer patients as the nature and cause of the pain differs both within and between patients. Consequently, we undertook a randomised, double-blind study comparing the effects of morphine and M6G in normal volunteers. We found that M6G had an analgesic potency three times that of morphine, but induced fewer respiratory problems, and less vomiting and sedation.

The major route of morphine administration in the treatment of pain is with oral preparations, but around that time, the use of nebulised (vapourised) morphine for the treatment of breathlessness was gaining favour. Therefore, in a subsequent randomised clinical trial, a new Research Fellow, Carol Davis, compared the effects of nebulised morphine and M6G in patients with chronic obstructive airways disease. After M6G, there was a significant improvement in exercise endurance, while morphine was no different from saline. Another Research Fellow, Columba Quigley followed this up in a phase I/II evaluation of nebulised M6G in cancer-related breathlessness, which showed that M6G was safe and of therapeutic benefit in this setting.

It would be nice to report that M6G is now licenced for the treatment of pain, but it is not quite there yet. A large randomised European study has confirmed the analgesic activity of M6G in the treatment of postoperative pain with limited side effects, and the compound is currently undergoing further clinical development with a company, PAION AG. Such is the length of time it takes for new discoveries to make it into clinical practice

In 1990, the solid tumour beds were moved from the Homerton Hospital back to the Barts site, so we again packed up our equipment and followed, finding a new home next to Clinical Pharmacology. We were greatly helped in this by Peter Wrigley, who introduced to the lab Norah Reed, the wife of a patient who had recently died of leukaemia. Norah got the fundraising bit between her teeth and has never looked back, raising £100K in her first fundraising year, a sum that funded the fitting out of our new labs at Barts. Norah continues to

fundraise for the BCI.

My own ambition for several years before this had been to be involved in clinical pharmacology studies in haematological malignancies, something that was easier on the Barts site as that was where the Haemato-oncology patients were treated. This ambition soon came to fruition. In lymphoma, we conducted a phase II study with a new drug, a proteasome inhibitor, carried out by Sandra Srauss, with Andrew Lister as the PI. In the lab, Sandra (with Lenushka Maharaj) used a primary culture assay system developed in John Gribben's lab at the Dana Farber and brought back to Barts by Peter Johnson. This was used to determine the sensitivity of primary lymphoma cells from trial patients to the agent under study and found an excellent correlation between *in vitro* sensitivity and clinical response.

The myeloma studies arose from a walk on the beach at North Berwick in Scotland, the site of the department's periodic academic retreat. Between sessions, Jamie Cavanagh and I were getting some exercise while discussing potential studies for a myeloma Clinical Research Fellow (Rakesh Popat). A new combination regimen with the proteasome inhibitor PS341, Adriamycin and dexamethasone was borne, with the snappy acronym PAD. This study went particularly well, due in no small part to Rakesh's endeavours.

In summary, we were all hugely enthusiastic about what we were doing, none more so than Maurice Slevin. I could always expect a phone call from him on a Sunday evening to discuss what was happening in the lab and to formulate an action plan for the week. His goal for me was to toughen me up. His usual mantra was "there are no prizes for nice guys!" Looking back on my time at Barts, I would say it was a pleasure and a privilege to have been part of the team, at a Group, Department and Institute level.

Paediatric Oncology

Sir John Lilleyman
Professor Emeritus,
Ridgwell Chair of Paediatric Oncology

I spent three different times at Barts – as a student from 1963 -1968, as a junior doctor in Paediatrics (1969-70), and as professor of Paediatric Oncology from 1995 – 2004. My fondest memories are from the undergraduate days when the hospital was a proud independent institution with an extraordinary heritage. Many of the senior medical staff were immortalised (if thinly disguised) in Richard Gordon's "Doctor in The House" books. Forty years later, as one of the senior staff myself, I watched its metamorphosis as the twin drivers of change – NHS re-organisation and centralisation of tertiary medical care – altered forever its repertoire and traditions.

The most memorable character I met at Barts was while a junior doctor working on Lucas and Kenton wards. Sister Kenton (all Barts ward sisters went by the ward name) stood at around five feet tall and ate medical students for breakfast! She stood no nonsense from medical staff of any rank, and at my level I was simply expected to do as I was told. Once this was understood, a friendship developed between us as I gradually appreciated her total focus on the welfare of her children on the ward. Many had cancer, some solid tumours and many with leukaemia, about which she knew everything and (at that stage) I knew very little. She was to be found in her office seven days a week and often late into the evening, plying distressed parents with tea and understanding. A most remarkable lady.

At around only 1600 new cases per year in the UK, childhood cancers pale into insignificance when compared to those in adults, but the evolution of their treatment has had a disproportionately large effect both on understanding malignant cell biology and demonstrating the value of large multicentre clinical trials. Barts has played its part in this growth of knowledge.

The story begins in 1948 with an article in the *New England Journal of Medicine*. Sidney Farber and colleagues in Boston described a small group of young children with the then invariably progressive and fatal acute lymphoblastic leukaemia (ALL). They all received a new anti-folate drug, aminopterin, and

many responded with complete disease remission, albeit short-lived. This seminal report saw the dawn of chemotherapy, not just for childhood leukaemia, but also heralded its wider application to other paediatric (and adult) cancers. A raft of antimitotic agents appeared over the next thirty years, and their demonstrable effectiveness changed clinical practice and training and inspired much clinical and laboratory research.

Before chemotherapy was widely used, consultants specialising in cancer (at any age) were confined to the still-newish specialty of radiotherapy and virtually no physicians or surgeons (adult or paediatric) were full time cancer specialists. There were no 'oncologists'. Patients were referred to radiotherapists, mostly by surgeons following biopsy or excision of localised disease. Which surgeons depended on where the lesion was sited.

This pattern of primary management for many localised or bulky cancers continued during the 1950s and early 1960s, and chemotherapy experience was being gained primarily in haematological malignancies. These, by their disseminated nature, are seldom controlled with localised surgery or radiotherapy. The early trials and therapeutic protocols for adult and childhood leukaemia and lymphoma were, therefore, developed by physicians and haematologists rather than surgeons or radiotherapists.

Early on the scene was a remarkable group of such pioneering physicians at Barts, during the 1960s under the guidance of Sir Ronald Bodley-Scott, an outstanding consultant appointed to the hospital in 1946. He had had a career-long special interest in haematological malignancy, and by the 1960s had become an international authority on the management of leukaemia and lymphoma. He was also a strong supporter of laboratory research into these diseases.

His team's focus on leukaemia spilled over to the paediatric wards of the hospital, Kenton and Lucas. Following the team's growing reputation, children with leukaemia were referred from a wide area to be treated with the latest experimental drugs at Barts with the help of the paediatricians.

Bodley-Scott's unit thus became one of the first *de facto* Medical Oncology departments in the UK, and one of the most influential, nationally and internationally. Trainees under his wing at that time read like a Who's Who of

the nascent specialty – including Gordon Hamilton Fairley, Jim Malpas, Tim McElwain, Derek Crowther and Ray Powles. It was towards the end of Bodley-Scott's illustrious career that my own first-hand memories of children's cancer at Barts began. Graduating from the hospital's Medical College in 1968, the following year I held a 6 month post-registration house officer post on Kenton and Lucas under Drs. Franklin and Cox (and Jackie Clark, the indomitable Sister Kenton). It was when I had my first hands on experience in the management of children with leukaemia. I worked under the supervision of Bodley-Scott's then senior registrar, Derek Crowther. I remember the ward rounds well, but it would be several years before my career returned to childhood blood diseases.

Elsewhere in the UK at that time, children with leukaemia were treated mostly by paediatric physicians in the larger children's units of major teaching hospitals (including Aberdeen, Newcastle, Belfast, Leeds, Nottingham, Oxford, Cardiff, Cambridge and Southampton) or regional children's hospitals such as at Glasgow, Edinburgh, Manchester, Liverpool, Sheffield, Birmingham and Bristol.

In London, Barts and Great Ormond Street (under Roger Hardisty, a haematologist) led the field, along with the new Royal Marsden Hospital at Sutton, which opened in the 1960s in addition to the original hospital in Chelsea and where Humphrey Kay developed an important paediatric leukaemia team. At that time, there was a very strong Barts/Marsden relationship with many staff from Medical Oncology moving between the two institutions (and the Marsden's Institute of Cancer Research) seemingly through revolving doors. There was much fruitful collaboration between the two institutions.

Meanwhile, in 1957, the UK Medical Research Council had set up a Leukaemia Steering Committee which, in turn, created a Childhood Leukaemia Working Party chaired by Professor J. H. Hutchison, with Humphrey Kay as its secretary. Its members were drawn from the involved clinical staff from the UK treatment centres outlined above. Under several subsequent chairmen, including Roger Hardisty, Tim McElwain and Tim Eden, and, with statistical support from Richard Peto's Clinical Trials Service Unit in Oxford, this committee developed and ran a series of consecutive clinical trials of evolving treatment protocols for ALL from 1960 for the next 40 years. Called the United Kingdom Acute Lymphoblastic Leukaemia (UKALL) trials, these documented a rise in the long-term disease free survival for afflicted children from 10-25% in 1970 to 80-85% by the end of the century. Importantly, the proportion of UK children with

ALL entering these trials over that period also grew from around 25% to 95% as successful outcomes ensured more complete referral to the collaborating centres. As the diagnosis of ALL splintered into disease subtypes from the 70s to the 90s, so trials for different subgroups were developed, and centralised diagnostic tests for genetic and immunological cellular features helped to define these groups. Successful trials for less common varieties of childhood leukaemia including Acute Myeloid Leukaemia (AML) were also carried out.

The treatment of other childhood cancers (the so-called 'solid' tumours), pursued a separate but parallel evolutionary pathway. Going back to the 1960s, surgery (for excision or de-bulking) and/or radiotherapy was the basic approach, with chemotherapy little used in primary therapy. This involved neurosurgeons for brain tumours, and ENT, cardiothoracic ophthalmic or orthopaedic surgeons for their anatomic domains, with paediatric surgeons for most of the rest including Wilms' tumours and neuroblastomas. Several NHS radiotherapy units developed paediatric expertise and the highly regarded department at Barts was a leader in this field, providing a service to Great Ormond Street as well as the hospital's own patients for many years.

Apart from a pastoral role, few paediatric physicians became primary co-ordinating therapists of solid tumours until the benefit of adjuvant chemotherapy became clear in the early 1970s. But there was no equivalent national forum to the MRC Childhood Leukaemia Working Party, no national clinical trials or central collection of data. Solid tumours were, therefore, less centrally referred, and often dealt with by a variety of system-specialist surgeons and physicians depending on the type of tumour involved. Outcomes varied across the country.

So, in the early 1970s, Barts, where its well-established Medical Oncology Department (which included a substantial paediatric sub-section) was now under the leadership of Gordon Hamilton Fairley, together with the Royal Marsden (from where Gordon had come) and Great Ormond Street, took a major step forward by forming the Children's Solid Tumour Group (CTSG) between the three hospitals and pulling together a protocol book covering the research-based diagnosis, staging and therapy of solid tumours. Important contributors included Jim Malpas, John Graham Pole and Tim McElwain. The so-called 'Barts/Marsden' manual contained research-backed protocols for staging and treatment of the commoner childhood solid tumours, together with some useful guidance on the rarities. It became the unofficial bible for virtually

all UK paediatric physicians who were faced with such patients.

As chemotherapy played a greater role, more physicians specialised in managing the diagnosis, staging and therapy of children with cancer, and paediatric oncologists began to appear. They established a loose but effective national network for collection and dissemination of clinical data. Some had already specialised in the management of childhood leukaemia and merely extended their role. Others focused on solid tumours and worked alongside haematologists, who looked after children with leukaemia.

The informal solid tumour network was formalised in 1977 by the establishment of the UK Children's Cancer Study Group (UKCCSG) with 14 founder members from all over the UK (including Jim Malpas and John Graham-Pole from Barts). Its role was to co-ordinate and standardise treatment and to establish clinical trials for solid tumours in parallel with the MRC Childhood Leukaemia Working Party. It was funded by a series of charitable grants and donations.

As the group expanded to support 22 now established major UK children's cancer centres, it later offered inclusion to all relevant professionals (nurses, pharmacists, social workers, pathologists and others) in a rapidly growing specialty and by 2002 had over 400 members. Finally, in 2006, the UKCCSG merged with the UK Childhood Leukaemia Working Party (who had separated from the Medical Research Council in the 1990s) to form the Children's Cancer and Leukaemia Group (CCLG). The story continues.

Barts had another unique role in the management of children's cancer as an international referral centre for the management of retinoblastoma. This was driven initially by the ophthalmic surgeons at the hospital and their collaboration with the radiotherapists from the 1960s onwards. Latterly, when the role of chemotherapy became established, the paediatricians became involved. In the 1990s, the clinicians who took this service to the point of being the primary UK centre were John Hungerford (surgeon), Judith Kingston (paediatric oncologist) and Nick Plowman (radiotherapist - or rather clinical oncologist, as radiotherapists called themselves by this time, to distinguish them from medical oncologists), with funding for the service direct from the NHS National Specialist Commissioning Advisory Group. This catered for all UK cases and several from other countries.

Children's cancer at Barts had a further boost in the 1990s when the Ridgwell family founded a Chair of Paediatric Oncology. The inaugural holder, Tim Eden, took up his post in 1991 and set up substantial research funding, but three years later he was head-hunted by the Cancer Research Campaign to its chair in Manchester Unit, where he stayed until his retirement. Tim in his time at Barts obtained grant funding from the then Imperial Cancer Research Fund (now Cancer Research UK), and from the Knatchbull Trust for two clinical fellows and continued to play a major role in the Childhood Leukaemia Working Party – latterly as its chair.

I arrived to replace him as Ridgwell Professor at Barts in April 1995 and inherited a small but dedicated and hard-working team, providing excellent clinical care and producing some interesting and original research. I was supported by Judith Kingston, my fellow consultant, without whose breadth and depth of experience, coupled with unstinting conscientious hard work, I would have been struggling since I had already begun to be dragged into a growing role with the Royal College of Pathologists. I did manage to expand the research funding to include further research fellowships, and over the next 2-3 years several substantial clinical and laboratory reports were published.

But as the 20th century drew to a close, the clinical management of childhood malignancy, growing ever more complex and demanding, threw up serious challenges for the Barts team in terms of service funding (as opposed to research funding), staffing and facilities. Chemotherapy protocols were becoming more intensive, leading to the need for more supportive care and demanding out-of-hours cover by experienced specialist staff. The growing role of stem-cell replacement therapy made even greater demands on in-patient facilities and staff expertise. It was obvious that Paediatric Oncology units like those at Barts and the Marsden, not being based in major children's centres for historical reasons, were increasingly challenged by lack of other on-site paediatric specialties, particularly intensive care, specialised surgery, renal medicine, imaging, pathology, haematology and biochemistry. The children's cancer unit at Barts was getting round these problems as best it could, with non-NHS funded research fellows covering out of hours, and "blue-lighting" children to the paediatric intensive care units at Great Ormond Street or Guy's hospital as crises arose. But the situation was far from ideal.

Such arrangements might nevertheless have lasted a while longer, but other challenges arose from a series of external political and financial pressures which

conflated to produce seismic changes in the configuration of Paediatrics in North East London.

The decision to merge Barts and The Royal London Hospital (RLH) into a single NHS Trust was followed by a major rationalisation of Paediatric services in the East End, including the closure of The Queen Elizabeth Hospital for Children in Hackney (QEH) - hitherto an outpost of Great Ormond Street for secondary children's services with only one specialist service - for children with sickle cell disease. In the late 1990s, this led to the relocation of all Barts Paediatric services (Kenton and Lucas wards and outpatients clinics, chiefly Oncology and Gastro-enterology) to the Royal London, along with the entire services from QEH following its closure. These migrating services coalesced with the resident paediatric teams at the Royal London. All this activity squeezed into the old building at Whitechapel, with Oncology being sited on the 4th floor in a considerably smaller ward than Kenton.

The clinical staff were crowded into small 'temporary' offices in an old nurses' home across the road. We were now further away from emergency tertiary paediatric services (neither QEH nor RLH had a paediatric intensive care unit nor was one likely to be approved). The site was less convenient for the laboratory research being pursued by our ICRF clinical fellow Vaskar Saha with Bryan Young at Charterhouse due to the increased distance between hospital and lab. Many patients and families found access by public transport to Whitechapel more difficult and expensive than travel to Smithfield. But everyone buckled down and life settled into a similar if less comfortable pattern as the 20th century drew to a close.

The next major event was a clinical catastrophe when there was an outbreak of pulmonary aspergillosis in the Oncology ward. This affected several children with myelosuppression and neutropenia and arose intermittently over a few months towards the end of 2002 until the pattern became clear. Some children very sadly perished. Every effort was made to discover the source, but in the end the microbiologists concluded that it was because of the contaminated fabric of a very old building. In the interests of patient safety and at my own insistence, it was decided towards the end of 2003 that the unit would have to close, at least temporarily, until new accommodation could be made available. The patients and specialist clinical staff were transferred to Great Ormond Street (younger children) and University College Hospital (older children). Only the retinoblastoma service was retained.

Newer, better accommodation was promised for the service to return, but expensive refurbishment of part of the old RLH with plans for the new hospital already well under way seemed unattractive, especially as the primary cause may not be eliminated.

'Temporary' arrangements in the NHS have a habit of rolling on and on. It was increasingly obvious to outside observers that Whitechapel was not a good place to develop a modern tertiary service in Paediatric Oncology, and that there was no support for it from NHS strategists. So, at the end of my clinical career in 2004, I left to work on full-time secondment at the National Patient Safety Agency as its Medical Director. Shortly afterwards, I resigned from my Chair at QMUL, and was not replaced. I finally retired from the NHS in 2007.

Judith Kingston is now a consultant paediatric oncologist at Great Ormond Street, but still works with Victoria Cohen (ophthalmic surgeon) and Nick Plowman (clinical oncologist) at Barts/Royal London providing a continuing service in retinoblastoma. This work is now shared with Birmingham.

The Paediatric Oncology research fellows from Barts/RLH progressed respectively to (1) a Cancer Research UK Chair of Paediatric Oncology in Manchester (Vaskar Saha), (2) a consultant Paediatric Oncology post at the Royal Marsden Hospital (Donna Lancaster) and (3) consultant Paediatric Oncology posts at University College London Hospital (Arnath Shankar and Sara Stoneham).

So, in summary, Barts contribution to paediatric cancer care and research has been remarkable over the last half of the 20th century but, apart from retinoblastoma, has run its course. The tertiary service in Paediatric Oncology took off in the 1960s and peaked in the period 1970 – 1990, latterly struggling with increasingly intensive therapeutic protocols and isolation from adequate specialist support services (especially paediatric intensive care). Matters worsened following a destructive reorganisation of paediatric services in East London at the end of the century which re-located the clinical service to the old building in Whitechapel. A major adverse clinical event occurred in 2003 precipitating the 'temporary' re-siting of the clinical service to Great Ormond Street and University College Hospital, and it has not returned. To date only the retinoblastoma service takes tertiary referrals at Barts/RLH.

These are the facts as I remember them. Despite the downbeat end, I regard my time in the Chair at QMUL and as a consultant at Barts/RLH as an honour and a privilege.

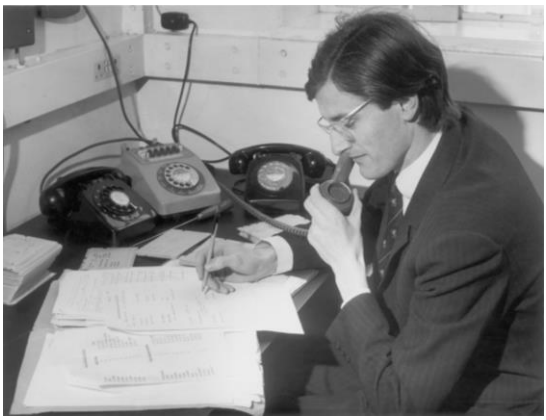
Male Genito-Urinary Cancer

Tim Oliver
Professor Emeritus, Medical Oncology

Having come to The London Hospital from Cambridge, my first link with Barts was through Marcus Setchell, a fellow Cambridge Student who chose Barts, though at that time I also made connections with other Barts students through social societies and sports, mainly golf. My career defining moment as a student came when I joined two other London Hospital students on an expedition to the South of France in a battered VW to spend two months as the first group of students to be sent on a student elective, which Marcus tells me did not happen until much later for Barts students.

Despite being hardly able to speak French, despite 6 years at schools, we soon learnt. I was fortunate to be allocated to the Haematology Professor Jacques Ruffie who was one of the few people who spoke English. He put me to read his publications on Immunology. As this was not a topic taught to undergraduates in the 1960s, I was able, after two months, to end up knowing more than the other students and most of my teachers! Once qualified, I so impressed my consultants during my house jobs, David Pennington, Wallace Brigden and John Blandy, that they put my name forward for a junior MRC Clinical Research fellowship, working with Hilliard Festenstein in the newly-funded transplant immunology unit with clinical attachment to the Renal Unit.

My role in the MRC Fellowship was initially to undertake animal studies of graft rejection, but when my innate lack of surgical skills became apparent, my primary role became setting up a collaborative exchange of kidney grafts to find the best match initially in London, but ultimately throughout the UK and Europe. This involved me in setting up a computer-based matching system using the Elliot 603 computer (see photo below) recently installed at The London and visiting all the London Renal units starting with Barts, which led to my forging a close relationship with Bill Cattell, Larry Baker and Bill Hendry. They all became close colleagues when I was later to join the Barts Leukaemia Unit at the end of my MRC fellowship. This happened because, as a result of late cancers developing in kidney transplants due to Immunosuppression, I became interested in trying to explore the potential of immunotherapy as an adjunct to cancer treatment.



Despite a complicated "ticker tape" programmed Elliot 603 at my disposal, in practice matching was done through punch cards and needle selection shown in this image from my office in 1971

As well as working on the kidney exchange programme, I became involved in HLA workshops which were International collaborations for defining new HLA antigens and defining their frequency in different populations and different diseases.

An earnest debater at an International HLA meeting in Paris 1971 "Un homme qui dit la verite" as was written on this photo by Mde Columbani my lab collaborator seen on my left who taught me how to do HLA typing using complement fixation test

These studies enhanced our understanding of the relevance of immunology in understanding resistance to cancer and was a major factor in my being accepted into the Barts Immunotherapy programme. However, before the Barts Immunotherapy post became advertised, I was fortunate in developing a collaboration with a Registrar in Radiotherapy, Christopher MacKenzie, while getting experience working in Radiotherapy Clinics. We investigated the immunosuppressive lymphopenia after radiotherapy in breast cancer patients, which others reported possibly explained accelerated metastasis, and resulted in no overall survival advantage compared with surgically treated patients, despite significantly reducing local chest wall recurrence. This experience, and

the exposure to patients in the Radiotherapy clinics I attended during this period, helped me considerably when I subsequently left the Leukaemia immunotherapy programme and began my final career in Urological Cancer.

When I finally left The London Hospital for the first time, my clinical research fellowship was under Gordon Hamilton Fairley. My post had originally been proposed to be a nursing post, but due to a misprint (!) converted into a clinical research fellowship post, with responsibility for looking after patients with Acute Myeloid Leukaemia undergoing immunotherapy. I joined Andrew Lister, harvesting the leukaemia cells from patients at the time of diagnosis using the cell separators. The cells were irradiated and given back to the patients when they were in remission, combined with weekly BCG, given by a 20 needle Heaf Gun. The cell separator was also used to collect platelets from normal donors for supporting the patients while they were undergoing remission induction chemotherapy. Initially, I worked under Ray Powles, who ran the Joint Barts/Marsden immunotherapy research programme with Peter Alexander at the Marsden. Subsequently, Ray went full time at the Marsden and I took over his post as Senior Scientific Officer, running the Barts Lab, developing trials and studying *in vitro* studies of the immune response in Cancer. These were used to monitor the clinical trial patients, but I also was able to continue my work studying HLA associations with cancer. I also took over supervision of Fran Balkwill, doing pioneering work on differentiation of leukaemia *in vitro* and Su Kim Lee, whose skill in *in vitro* culture of immune cells from patients, gave us the possibility to demonstrate the relevance of self HLA transplantation antigens in leukaemia immunotherapy. This led to the novel design of the Barts VII trial, which I initiated during the year. I also ran the ward, while Andrew was seconded to Harvard. This gave me the experience of using chemotherapy in the primary treatment of leukaemia, though the trial became a casualty of the aftermath of the death of Gordon Hamilton Fairley at the hands of the IRA. The loss of this great man was difficult enough to bear, but it was also a catalyst for my own misfortune. I was preparing to do a secondment to Houston, but instead lost my job due to the re-organisation that took place, with the appointment of Jim Malpas as Head of Department, whose work was principally with childhood cancer.

Fortunately for me, this was the time of rapid progress in chemotherapy of testicular cancer and a breakthrough in the use of immunotherapy with BCG in bladder and kidney cancer. This resulted in my former Urology colleagues in the field of transplantation, looking for an Oncologist to develop a programme of collaborative clinical trials between the Institute of Urology, the Institute of

Cancer at the Royal Marsden, The London and Barts led by Julian Bloom. Through this post, I re-joined John Blandy, who had been actively involved in the development of the London Hospital Kidney

With Julian Bloom and his then registrar Alan Horwich at the end of a joint ward round

Transplant programme and was developing plans to relocate the Institute of Urology into The London Hospital. Jim Malpas was instrumental in getting me the post, after I had done an accelerated tour of US centres to get experience in the field of Uro-Oncology. Because of the rarity of testicular cancer, which up until that time had been looked after by radiotherapists, it was agreed that I would look after the patients from Barts, The Royal London and the Homerton Hospital, the then newly opened solid cancer Oncology centre for East London. This meant I continued a connection with the ICRF unit at Barts, but I spent a large amount of my time commuting between clinics in East London. This link proved of particular benefit when my unit was transferred to The London, as this occurred without any NHS support because the Institute staff had voted to move to the nearby Middlesex hospital. This occurred at a time when my first breakthrough in treatment of testis cancer led to my getting ICRF support for trials of single agent Carboplatin in Seminoma and begin studies of the genetics of testis cancer.

The move occurred at a time of exciting new research in prostate cancer and Jim Malpas seconded Jonathan Waxman to work as an honorary senior registrar

with my unit, while developing his studies in the use of medical castration with Gonadotrophin-releasing hormone agonists instead of surgery for patients with metastatic prostate cancer. He pioneered a nasal compound that selectively blocked the pituitary production of the hormone, regulating gonadal production of testosterone and also explored their potential in protecting the gonad from chemotherapy damage. On the basis of this work, he gained a prestigious Senior Lectureship at the Hammersmith and Chris Gallagher joined my unit from Barts. He developed a research programme in endocrine treatment of breast and ovarian cancer and became the Unit's first senior lecturer. In addition, he also did pioneering work investigating prolactin blocking drugs in prostate cancer. As a result of this expanding work, the ICRF grant was increased at my first quinquennial review and, with matching funding from The London, a laboratory programme was developed. This included the attachment of a postdoctoral fellow, Ahmed Nouri from Hilliard Festenstein, to investigate loss of HLA expression in bladder cancer as a mechanism for escape from BCG-induced immune control and to do *in vitro* studies of gene therapy to try and translate the successful studies Hilliard Festenstein had undertaken with similar gene therapy correcting H2 loss in murine lymphomas.

Sadly, my second quinquennial review fell at a time when there was an economic recession and the ICRF had financial problems. As a consequence, my relatively small programme was shut down at the time when the NHS was transferring Cancer Services to Barts, and it was only possible to salvage the testicular cancer trials programme, in part due to a donation from a personal foundation (The Stadium Trust) in memory of a patient I treated at the London Hospital.

Jonathan Waxman and members of my London Hospital team at our summer party 1985.

Despite the setback prior to the Barts/London Medical Oncology Units merger, once the dust settled, the extra space and facilities enabled considerable expansion of the Testicular Cancer Trials programme. We were also able to develop the NHS solid cancer Medical Oncology Unit, which expanded our interests in prostate cancer through the efforts of Peter Wrigley, who set up the Prostate Cancer Charitable Trust with one his patients Clive Bourne. The setting up of the Anglian supra-regional teleconference network throughout Essex, Cambridgeshire, Suffolk and Norfolk became a testing ground for pilot studies and the successful studies became MRC National studies.

Trustees of Prostate Cancer Charitable Trust. Left to right Roger Kirby, Myself, Dirk Bogarde, Peter Wrigley, Clive Bourne, Michael Bentine, Arie Belldegrun and Shirley Claff

In addition, our salvage chemotherapy programme, undertaken in collaboration with Andrew Lister's autologous bone marrow transplant programme, was very successful in salvaging even the most resistant patients and, by 1997, we were able to publish the then best overall results in a testicular cancer, which is now standard across the country, with 97% of all patients becoming long-term cures.

Hearing of this success and the problems with funding, one of the successfully cured transplant patients, Colin Osborn set up the Orchid Cancer Appeal and with the help of generous support from The Stadium Trust, our level of funding

increased to £1million a year. With this support, we were able to reinstate the laboratory programme under Yong-Jie Lu, studying the genetic basis of the chemo-sensitivity of Germ Cell tumours and cytogenetics of prostate cancer, and develop assays to study circulating prostate cancer cells in the blood. We were also able to reinstate our senior lecturer post which had been lost with the merger, appointing Jonathan Shamash.

He had made a significant contribution to the success of our autologous bone marrow transplant programme and other aspects of salvaging the rare failure of standard chemotherapy and re-launched our prostate cancer endocrinology programme, re-appraising the role of testosterone in prostate cancer differentiation. In addition, three highly successful clinical research fellows, Tim Lane, Tom Powles and Greg Shaw, undertook thesis projects linking clinical trials and our laboratory programme, which enabled them to go on to successful clinical careers. David Prowse, who helped Greg Shaw with his lab research, went on to be a successful senior lecturer. Finally, we were also able to contribute 50% to the salary to support Dan Berney, developing his career as an academic Uro-Pathologist. This year, because of this work, he was appointed as Professor in Uro-Oncology Pathology. His International Academic reputation in the pathology of testicular, prostate and penile cancer is quite unique and particularly from his studies in penile cancer (a particular interest of mine ever since my proposal to vaccinate all males against HPV at Puberty in 1994 was turned down!), but is now finally becoming mainstream and strengthened through Dan's work

In September 2006, I organised a one day meeting, examining the long view of priorities for the future in fields where I planned to retain an interest in, inviting colleagues from around the world, ending with an evening of music from John Lumley's Choir, singing Gounod's St Cecilia's Mass and then a celebration feast in No 1 St Mary Axe "The Gherkin". On 6th October, I finally retired from my Chair and my NHS role, with Jonathan Shamash taking over responsibility for Testis and Prostate Cancer, while Tom Powles took over care of my practice in Renal and Bladder Cancer.

With the London East End having just been announced as the venue for the 2012 Olympics, I decided to postpone my academic retirement for 5 years and work "pro-bono" on trying to understand why exercise prevented all causes of cancer mortality, with joint appointments with Jack Cuzick in the Wolfson institute and Peter Hamblyn in Sports Medicine. Very quickly it became apparent that

sunshine was a confounding variable in all exercise health benefits and this has become the topic of my CRUK Grand Challenge proposal and the focus of my second "post-retirement" quinquennium. This will be run jointly with the Orchid Appeal and aims to raise funds to monitor the impact of Orchid's community sports education project on cancer awareness and cancer prevention. As part of this programme, we are aiming, in association with SNAG golf organization, sponsorship of an internet based community Olympiad to coincide with the 2016 Olympics.

The Orchid Cancer Appeal has continued to grow in the nine years since my retirement and through its support for research in penile and testis cancer is now developing a National and International presence. One final area to keep me off the golf course will be completing the 20-year follow up of Carboplatin studies in testis cancer and 10-year follow up of my Intermittent Hormone Therapy studies, which have had an initial presentation in conferences in the last year.

Gynaecological Oncology

John H Shepherd
Professor, Surgical Gynaecology

Contributions from Dr Arjun Jeyarajah MD MRCOG, Barts Health NHS Trust

I was appointed to the consultant staff of Barts in 1981 by Gordon Bourne, the then head of the Obstetrics and Gynaecology Department, making me the first formally trained British Gynaecological Oncologist. For this, I am indebted to Gordon, who had foreseen the need for subspecialisation and the development of expertise in different areas of gynaecological practice, hence my appointment.

Having completed a general surgical training as a fellow of The Royal College of Surgeons of England, prior to taking up Obstetrics and Gynaecology, I had undertaken an American Cancer Society Fellowship programme as a Fulbright scholar at the University of South Florida in Tampa, under the supervision and tutorship of Dr Denis Cavanagh. This American model of subspecialist training not only included instruction in advanced pelvic and abdominal surgery, but also included radiotherapy and medical oncology. When appointed to the staff at Barts, there was only one other department, at The Queen Elizabeth Hospital in Gateshead, which had a department of Gynaecological Oncology, originally conceived by Stanley Way in 1948, and subsequently taken over by his protégée John Monaghan.

The department of Gynaecological Oncology at Barts also had a rich tradition going back to the 1940's when John Howkins, who had trained under the great Victor Bonney, continued to develop his technique for pelvic and abdominal surgery whilst on the consultant staff at Barts. Howkins promoted the development of gynaecological surgery in a strong surgical department at Barts, which at the time had also introduced the first radiotherapy machine for external beam teletherapy. Howkins was joined by Christopher Hudson, who subsequently took on the mantle of pelvic cancer surgery from Howkins when he retired in 1967. Hudson should be credited with the first surgical description of the retroperitoneal approach for the radical excision of a disseminated pelvic ovarian malignancy, a modified version of which continues in use to this day.

Others who joined Barts include Donald Fraser, Gordon Bourne, David Williams and Marcus Setchell.

Returning to the 1980s, the development of Gynaecological Oncology at Barts had begun and was modelled on the training programme I had received in Tampa, bringing together all competing cancer specialties, both surgical and non-surgical. It was a dynamic and challenging time, as we worked on what was then an innovative approach to the management of patients with gynaecological malignancies in the UK.

Nurses on the gynaecology ward

I worked initially with Dr John Whittle (Consultant Radiotherapist in Professor Arthur Jones' department), and subsequently Dr Sidney Arnott, who moved from Edinburgh to London. Dr Peter Wrigley (Consultant Physician and Medical Oncologist in Professor Jim Malpas's department of Medical Oncology) identified his then senior registrar, Dr Maurice Slevin, to work in collaboration. We were fortunate to be supported by excellent diagnostic specialties, with Dr Arthur Stansfield (Consultant Histopathologist), with a particular expertise in solid cancer pathology, and Dr Marigold Curling (Consultant Cytopathologist). In radiology, Professor Rodney Reznek and Dr Judith Webb, were crucial members of the team, providing much interdisciplinary rapport with healthy discussion, if not occasionally argument, at the weekly meetings! A crucial non-medical member of the team proved to be Hilary Everett, a medical social worker from the well-established Almoner's department at Barts. She recognised the need for adequate counselling and support, not only for women afflicted by gynaecological malignancy, but also their families who needed help

in coping with difficult and sometimes tragic circumstances. Her work, together with that of Dr Mary Crowther, which resulted in a *British Medical Journal* (BMJ) publication, was one of the earliest to define the holistic needs of gynaecological cancer patients. As a result, the first McMillan-funded clinical nurse specialist, Rachel Hamer, was appointed at Barts, working with Gill Taylor, the Senior Gynaecology Nursing Sister. Finally, in recognising the essential need for palliative care expertise, Dr Theresa Tate was appointed to the consultant staff, together with her senior registrar and now consultant, Dr David Feuer.

With this infrastructure in place, a fellowship teaching programme was established, initially with Australian and European fellows, who were self-funded, the first two fellows being Dr, now Professor Bruce Ward from Brisbane and Dr Mary Crowther. We subsequently worked with The Royal College of Obstetricians and Gynaecologists (RCOG), which at that time was developing the recognised subspecialties including Gynaecological Oncology. This resulted in RCOG recognition as the second UK official Gynaecological Oncology subspecialty training programme, with the first official fellow being Dr Thomas Jobling, now Professor of Gynaecological Oncology in Melbourne, Australia. The programme expanded in conjunction with the Royal Marsden Hospital, where I had been appointed Consultant Surgeon in 1983, and became the largest training programme in the UK, with two recognised fellows at any one time. Further expansion of the training programme occurred in 2002, when a third clinical/academic fellowship programme was established at Barts. The Barts and Barts/Marsden Gynaecological Oncology Fellowship Training programmes have an international reputation, attracting trainees from Europe and beyond. Among the 35 to successfully complete the programme and challenging course in one piece are Professor Hextan Ngan, Hong Kong; Dr K.F Tham, Singapore; Professor Peter Van Dam, Brussels; Professor Phillipe Van Trappen, Bruges; Professor Ian Jacobs, Sydney; Mr Jonathan Herod, Liverpool; Mr Rick Clayton, Manchester; Mr Tim Mould, UCLH; Mr Thomas Ind, Royal Marsden and St George's; Mr Robin Crawford, Cambridge; Mr Robert Tozzi, Oxford; and, of course Mr Arjun Jeyarajah, Barts!

The department has traditionally had strong links with basic science and translational research. Beginning in the 1940s, Wilfred Shaw established the Williamson laboratory in the basement of the East Wing, which was run by Bert Cambridge, and was the focus of research activity, with several trainees carrying out their laboratory research there. The dedication of this lab is best summed up in an acknowledgement by Wilfred Shaw in his BMJ publication in

1949 "Our thanks are due to Mr. Bert Cambridge, of the Williamson Laboratory, for his great help, particularly in sorting out microscope slides from bomb debris"!

This medical school laboratory continued with clinical and academic research in both cancer and fertility, subsequently moving to William Harvey House and the department of Human Reproductive Physiology, under the supervision of Professor Timothy Chard. Several research fellows within the department have completed MD and PhD theses within this environment. With the development of the Charterhouse Square site, after the move of the ICRF laboratories to the site and the arrival of collaborators including Professors Nick Lemoine and Fran Balkwill, the translational research activities of the department have centred at Charterhouse Square within the Barts Cancer Institute.

In terms of clinical research, impact in gynaecological radiology would be one of the most notable achievements at Barts, with Rodney Reznek, an international authority on pelvic imaging, leading on protocols and guidelines not only for ultrasound, but also CT and MRI, which have resulted in international recognition and multiple ground-breaking scientific publications. This also allowed our research fellows to develop joint research projects, which subsequently led to new techniques, which subsequently became established as standard practice. Collaborative work with Rodney on subjects such as case selection for fertility-sparing surgery for early cervical cancer, have made a significant impact on clinical practice (more details can be found in his contribution). Several radiology staff such as Dr Aslam Sohaib (Royal Marsden Hospital), Professor Andrea Rockall (Imperial College) and Dr Anju Sadhev (Barts) have trained in the department in pelvic imaging and have been appointed to major institutions.

The 'modern' era of the Department was defined by the merging of the departments of Gynaecological Oncology headed by David Oram at The Royal London (RLH) and myself at Barts in 1994. This was as a result of restructuring within the NHS that led to The Royal London Hospital and Barts joining to form one Trust. As one might expect from such a NHS merger, there were several political ramifications that affected many departments adversely. Many had predicted a rivalry between the RLH and David Oram with Barts and myself, but nothing could have been further from the truth.

Management had requested and expected the service to contract, but in a

moment of serendipity, David moved next door to me in Dulwich Village, 6 months before the merger. This allowed us to plan our amalgamation, to expand not contract the department, over the garden fence with a bottle of Sancerre! We went from strength to strength. Our two departments embraced the challenge, thus forming the largest and busiest clinical service and fellowship training programme in the country. Considering the chaos and catastrophic failings that follow so many NHS restructures, this could arguably be viewed as almost a unique achievement or victory against the bureaucrats!

Ian Jacobs was the subspecialty trainee at the RLH at the time and moved with David Oram to become the first combined trainee in the department. He was subsequently appointed as a Senior Lecturer and then Professor at Barts. He moved to UCL and then to Manchester, and has recently been appointed Vice Chancellor of the University of New South Wales in Sydney, Australia

David's interests centred on ovarian cancer screening and carcinoma of the uterine corpus, and with Ian Jacobs, brought with them their established research programme into the multimodal screening for ovarian cancer, using tumour markers and ultrasound. This subsequently developed into the multicentre UKCTOCS prospective randomised trial into screening for ovarian cancer, for which Barts remains the highest recruiter, with approximately 10% of all 200,000 participants. The results will establish how many lives can be saved by ovarian cancer screening, and help inform decisions on any future national screening programmes. As an indicator of how long research can take, the final results for this study, which began in 2001, are due out in late 2015, though preliminary analysis has suggested that screening has encouraging sensitivity in detecting ovarian cancer.

My own group's research focus was cervical cancer, both (i) early cancer of the cervix for which we developed and expanded fertility-sparing surgery by means of radical vaginal trachelectomy and laparoscopic pelvic node dissection, and (ii) the challenge of recurrent and progressive cervical cancer requiring pelvic exenteration and reconstruction (once made more "challenging" when hospital management scheduled the exenteration in a dental theatre!) This work resulted in a Hunterian Professorship at the Royal College of Surgeons in 2005.

With the introduction of cancer networks as part of the Calman-Hine ethos of structured cancer care, Barts was designated the regional centre for the North East London Cancer Network. Arjun Jeyarajah was appointed in 1999 to

develop this further and chair the network, which has led to a huge expansion in the clinical service at Barts. The consultant staff has now expanded to include five surgical gynaecological oncologists and the department is a supra regional centre for fertility-sparing surgery for early cervical cancer and ultra-radical surgery.

The team's medical oncology service was further developed by Dr Christopher Gallagher, who also moved from the RLH to Barts following the merger. Subsequently, Dr (now Professor) Ian McNeish joined us at the advent of the Barts Cancer Institute in 2004, moving to Barts with Professor Lemoine's group. Iain was instrumental in developing the clinical and academic profile of the Medical Oncology service, and is now Professor of Gynaecological Oncology, at the Institute of Cancer Sciences, University of Glasgow. The Clinical Oncology or radiotherapy services were originally directed by Dr Sidney Arnott, and he was succeeded on retirement by Dr Melanie Powell. Histopathology collaborators include Drs Naveena Singh and Asma Faruqi.

Recently, the department has seen several changes. With the restructuring of health care in North East London, all major surgical specialties, including Gynaecological Oncology, have been moved to the Royal London site. This move has been embraced by the department, which has managed to maintain its staffing and clinical provision. The new Royal London Hospital presents a modern, up-to-date facility and with the co-locations with other surgical specialties, the challenge to deliver an even better service is apparent.

There are two other achievements that should be mentioned. The first was BACUP, which was founded from the close relationship between Maurice Slevin, myself and Vicky Clement Jones with her husband Tim, now Lord Clement Jones. As mentioned by Peter Wrigley and Jenny Ellwood in their chapters, Vicky was one of our patients but also a doctor at Barts, who had the vision and determination to set up the first national cancer information service for patients, so shocked was she at how little basic information was available even to herself, a doctor. This service is now part of MacMillan Cancer Support and serves as the perfect memorial to Vicky, who sadly died of ovarian cancer at the age of 39 in 1987.

The other is the contributions made by Barts to the "gynae bibles", the text books used internationally to teach students, Bonney's Gynaecological Surgery and Shaw's Textbook of Operative Gynaecology and Gynaecology. Bonney's

was first published in 1911 and Shaw's in 1953, shortly after Wilfred Shaw's death at the age of 55. These remain undoubtedly the leading gynaecological textbooks worldwide, and so it is important to mention the contributions by Barts', with John Howkins, who, being a prolific writer, was Editor of both textbooks, and other Editors for Shaw's including many of my fellow Barts surgeons mentioned in this chapter, Christopher Hudson, Marcus Setchell, Gordon Bourne & myself. In addition, Gynaecological Oncology (Shepherd and Monaghan) was first published 1985 and was the first European and British text book on the subject.

Looking back on my time at Barts, I would say that I view the development of the multidisciplinary "gynae-onc" team in the 1980s, as one of our greatest achievements at Barts, a precursor of what has become the accepted standard, multi-disciplinary team for the management of gynaecological malignancies.

Departmental reunion dinner upon my retirement, 2009

Professor Rohatiner makes the same point in her chapter on haematological malignancies. Each and every individual and the disciplines they represented were a crucial part of our development, and for my part, the three most important things I could impart to our team, which I had learnt from all my mentors, was competence, confidence and, most importantly, humility. That is the ethos on which our department was built, each individual being a crucial part of our development.

Cancer Imaging

Rodney Reznek
Emeritus Professor, Diagnostic Radiology

Contributions from Dr Anju Sahdev, Nuclear Medicine, Barts Health NHS Trust, and Professor Emeritus Peter Armstrong, and Professor Emeritus Stephen Mather

The concept of radiologists with a specialist interest in imaging patients with cancer is relatively recent. It is only over the past few decades that the need has arisen for specialist radiologists who are trained in a wide range of imaging modalities, who understand the history of cancer, are familiar with cancer treatments and prepared to explore the contribution that imaging could make to clinical trials. The Barts' radiological department has been central to the development of Oncological Radiology as an established specialty in many parts of the world. Together with Professor Dame Janet Husband, then from the Royal Marsden Hospital, I founded the International Cancer Imaging Society with the aim of promoting education and research in Cancer Imaging. This society now has about 60 eminent international Fellows, hundreds of members from around the world, has held 15 Annual Teaching Courses in cities around Europe, satellite meetings with other scientific societies around the world, and has a high impact factor online journal, *Cancer Imaging*.

The awareness of the need for specialist cancer imaging has been paralleled by the extraordinary recent advances in imaging, particularly over the past two decades. Ultrasound, Computed Tomography (CT), Magnetic Resonance Imaging (MRI), Positron Emission Tomography (PET) and interventional techniques have all revolutionised how patients are investigated, treated and monitored while under the care of oncologists. Such technology and associated research is of course expensive, and in many cases, particularly in the earlier years, its funding at Barts was generously provided by the Barts Special Trustees, external charitable trusts and the Barts Research Committee. Thanks to the foresight of those making such grants available, the often bewildering innovations introduced with imaging technologies have been available for clinical use and imaging research at Barts.

Advances in CT can be used to illustrate the evolution of this complex imaging

technology extremely well. In 1980, the Barts CT scanner took about 20 seconds to acquire the data for each axial 'slice' and about 20-30 minutes to process the data to produce the images of a typical body part such as the abdomen. The images were then photographed on to film for interpretation by radiologists. Accurate measurement was difficult, often measured from the film with a ruler and multiplied by a factor of 7 to translate into centimetres. These measurements were then fed into protocols to estimate changes in tumour size. Nevertheless, valuable studies into the staging of cancer, such as carcinoma of the stomach, lymphoma, testicular cancer and others were all completed. Under the guidance of Dr Ian Kelsey Fry, formerly Dean of the Medical School, and Dr Liz White, these studies proved to be an early model of how such careful prospective studies with surgical and pathological correlation should be conducted. Much early work on the place of CT in the staging and management of lymphoma was completed in close collaboration with Professors Andrew Lister, Ama Rohatiner, George Blackledge and Dr Chris Gallagher. The first Fellow responsible for the scanner was Adrian Dixon, who went on to become Professor of Radiology at Cambridge University (and then Master of Peterhouse College).

The introduction of a 'spiral' CT to Barts in 1993 dramatically altered the approach to CT scanning. The revolutionary technological difference lay in the introduction of a slip-ring gantry mechanism that no longer required a delay between scans. Unlike in its predecessors, where the gantry rotated around a stationary patient, in spiral (helical) CT the patient moves through a rotating gantry continuously producing X-rays. Multidetector CT (MDCT) introduced the ability to acquire data from more than one slice simultaneously, using parallel rows of detectors. Scanners are now capable of obtaining 4-128 slices in a single X-ray tube rotation. The entire chest, abdomen and pelvis can be scanned during 1 breath hold and the images processed in less than 2 minutes. These systems now can provide thin, < 1 mm 'slices' which allow high resolution sections, ideally suited to radiotherapy planning and treatment and response monitoring. 3D and 4D multiplanar reconstruction (MPR) and surface rendering have multiple applications including virtual colonoscopy shown to be of value in detection of mucosal lesions, particularly after failed colonoscopies or in elderly patients, virtual bronchoscopy and the depiction of the detailed shape of tumours. The input of renowned specialist gastrointestinal radiologists such as Dr Alison McLean and previously Dr Clive Bartram (who went on to become Professor at Imperial College School of Medicine) was invaluable in keeping the department at the cutting edge of gastrointestinal cancer imaging. 4D CT (3D plus movement synchronization) has also allowed

collaboration with radiotherapy colleagues for use in image-modulated radiotherapy (IMRT) in the treatment of several cancers, including prostate, lung, and head and neck cancers.

More accurate targeting through CT and ultrasound together with improved biopsy techniques facilitated research into image-guided biopsy techniques. Work done with Professors Rohatiner and Lister established image-guided core biopsy as a safe, effective and accurate technique for obtaining sufficient pathological material to manage patients with non-Hodgkin's lymphoma. Similar work done with Dr Judith Kingston of the Department of Paediatric Oncology showed that percutaneous biopsy provided sufficient information for children with abdominal tumours. In both settings, this became accepted widely as standard clinical practice, allowing more invasive interventions such as laparotomy or thoracotomy to be avoided.

Shortly after the introduction of Body CT, it was soon apparent that its reproducibility between examinations made it a valuable new marker as a surrogate endpoint for clinical trials in patients with cancer. As Professor Andrew Lister once pointedly remarked: "every CT scan we do is part of a research study." This insight became an additional motivation in striving to help not only with the care of individual patients, but also to contribute to the research work of colleagues.

The technological evolution of MRI over the past few decades was also reflected within the Barts Radiology Department. In the mid-1980s, a UK-manufactured MRI machine with a 0.08 Tesla magnet was installed with funding from the Department of Health. Only four such devices were ever installed. Images were of low resolution compared with machines with higher strength magnets, but the measurement of T1 relaxation times was remarkably reproducible, allowing diffuse changes to be accurately documented. This allowed research into various aspects of lymphoma. The MRI Unit was headed by Dr J A W Webb, an international figure in genitourinary radiology and the lymphoma MRI research was carried out with Professor Mike Richards, then working successfully toward his MD in the subject (later National Cancer Director and now Chief Inspector of Hospitals at the Care Quality Commission). The clinical applications of this magnet were of course limited and, fortunately, it was replaced in 1993 by a 1.5 Tesla scanner very generously funded by the Leopold Muller Trust based on a bid prepared by Professors James Malpas and Peter Armstrong.

Professor Armstrong headed this highly successful and innovative MRI unit. A series of outstanding research fellows conducted numerous cancer-related research projects in what became one of the first Oncological Imaging Research Fellowships. Many went on to occupy designated consultant posts in oncological imaging. These included Dr Aslam Sohaib at The Royal Marsden and Dr Anju Sahdev at Barts. A total of 16 have so far undergone training fellowships in oncological imaging.

Ground-breaking work on cancer imaging was carried out with a team of gynaecological oncologists led by Professors John Shepherd and Ian Jacobs and the input of Dr Judy Webb. The impact of this work was to alter the management of patients with gynaecological malignancy substantially in several types of disease. For example, the role of MRI in characterising adnexal masses was worked out by this team and algorithms based on these findings are used worldwide for the management of women with such pathology. Similarly, the value of MRI in selecting patients for uterus-conserving surgery in women with cervical cancer revolutionized the decision-making process in young women presenting with this condition. MRI research was given an added impetus with the recruitment of Andrea Rockall as senior lecturer, now Professor of Radiology at Imperial College. Professor Rockall's highly acclaimed study into the use of the lymph node specific contrast agent, ultra small paramagnetic iron oxide particles, in the detection of malignant lymph node infiltration in gynaecological malignancy, provided the basis for several other studies.

Another research thrust in cross-sectional imaging, conducted within the department for over three decades, has been the detection and characterization of neuroendocrine tumours. With enthusiastic collaboration over the years from Professors Mike Besser, Ashley Grossman, John Monson, Shern Chew, Will Drake and Dr Scott Akker, the team published over 50 articles in peer reviewed journals on neuroendocrine tumours of the pituitary, pancreas and adrenals.

More recently, the introduction of newer technologies at Barts, coupled with the necessary expertise, has allowed the department to provide state-of-the-art imaging information. For example, the arrival of a 3T MRI unit, and the use of novel imaging sequences with and without contrast agents, have provided improved imaging data and further research possibilities. These include tractography and blood oxygen level determination (BOLD) imaging. These

provide functional information (fMRI), echoplanar and MR perfusion and diffusion weighted imaging (DWI). The added value of diffusion weighted imaging (DWI) has been investigated in the detection of tumours; for example, endometrial, ovarian and pancreatic islet cell tumours and as a means of assessing disease response to treatment, thereby allowing both morphological and functional tumour response assessment. Dynamic contrast medium enhancement (DCE) has also shown promise in the evaluation of treatment response. Both these MRI innovations are currently being extensively studied by the MRI team, particularly in relation to renal cancer with Professor Tom Powles, cervical cancer with Dr Melanie Powell and ovarian cancer with Professor Michelle Lockley In the clinical setting, a combination of morphological and functional information from DWI and DCE imaging has been developed and applied to prostate cancer over the past 5 years. Before biopsy, this has improved cancer detection, guided prostate biopsy, enhanced tumour staging, been used in surveillance and in the assessment of disease response following chemoradiation. This multiparametric MRI for prostate and gynaecological cancers exemplifies the contribution that state-of-the-art imaging has made within the department, both to facilitate optimal patient management and to guide research. Similarly, whole-body MRI, combining T1 imaging and DWI offers great prospects for the detection and monitoring of bone metastases, particularly in the setting of skeletal metastases from breast cancer, prostate malignancy and multiple myeloma, all areas under investigation.

In parallel with these developments in the anatomical imaging of cancer, pioneering research in the early establishment of Molecular Imaging of the disease was taking place in the Nuclear Medicine Department at Barts.

In 1980, a conversation took place between Sir Walter Bodmer, Director-general of the Imperial Cancer Research Fund (ICRF) and Dr Keith Britton, Head of the Nuclear Medicine Department. Sir Walter pointed out that monoclonal antibodies, developed within the ICRF, reacted with tumour associated antigens, present on a variety of epithelial cancers. Dr Britton suggested that improved radiolabelling and imaging techniques could be applied to these antibodies for use in imaging these cancers in patients. As a result of this discussion, in 1981, Dr Aga Epenetos was supported by the ICRF as a postgraduate fellow in this department undertaking a PhD in this field. His initial work confirmed the selective uptake of the Iodine-123 monoclonal antibody, initially in implanted tumours in animals and subsequently in patients with ovarian cancer. In order to build on this initial success, the team

at Barts was expanded to include Dr Maria Granowska to undertake further clinical research and Dr Stephen Mather (now Professor Emeritus) to develop improved radiolabelling methods for monoclonal antibodies.

Steve Mather remembers that he first came to Barts to improve the method for labelling monoclonal antibodies with iodine-123. Before this time, antibodies had been labelled mostly with iodine-131 or iodine-125, but iodine-123 was potentially much better for imaging. The problem was that it was very expensive and, in addition, the labelling yields achieved using the methods previously used for I-125 and I-131 were very low – less than 10% - so most of the very expensive radioisotope went down the drain (safely, of course!). So why should I-123 behave so differently to the other radioisotopes of iodine – these are after all, the same element? Steve reasoned that because I-123 has a much shorter half-life than the others, the concentration of iodine ions in the solution would also be much lower – more than 10 times lower. So he tried increasing the concentration by adding a very small amount of stable iodide (I-127) to the I-123. The labelling efficiency went up to 70% or more! This made the imaging approach suggested by Keith Britton a feasible, rather than a theoretical proposition, and this early success was just what Steve needed to persuade him to move into research on a full-time basis at Barts.

In the 20 years following, with the support of ICRF and subsequently CRUK, Dr (subsequently Professor) Britton and his team established a world-wide reputation in the use of radiolabelled biomolecules for imaging and treating a range of cancers. A panel of antibodies from ICRF including HMFG2, PR1A3, SM3 were processed and radiolabelled in the Nuclear Medicine Research Laboratory, established by Dr (subsequently Professor) Mather to permit their use for imaging ovarian, breast and colorectal cancer. Collaborations were also established with the Pharmaceutical industry, in particular Cytogen, Antisoma (established by Dr Epenetos) and Coulter Pharmaceuticals to allow this work to be expanded to the imaging of prostate cancer and the treatment of ovarian cancer and lymphoma with targeted radionuclide therapy.

In further developments, the radiolabelling and imaging techniques, initially developed for use with monoclonal antibodies, were refined and applied to other biomolecules such as cytokines (for imaging autoimmune disease) and neuropeptides (for imaging and treatment of neuroendocrine cancers). Much of this research has since been adopted and further developed across the world and this discipline of molecular imaging and therapy has now become an

important part of Nuclear Medicine clinical practice.

Closer clinical and research collaboration between cross-sectional imagers and nuclear medicine practitioners was initiated by the introduction into the department of a PET-CT scanner in 2007, the first 64-slice CT time–of-flight scanner to be installed in the UK. Its clinical impact was immediate, particularly in the evaluation of patients with primary bronchial carcinomas, head and neck malignancies, lymphoma and melanoma. The unit was set up by Professor Norbert Avril, a nuclear medicine physician (now at Case Medical Centre, University Hospitals, Cleveland, Ohio) with a substantial clinical and research profile in PET-CT. Within a short time, projects were undertaken investigating the contribution of PET in urological cancers, lymphoma, lung cancer, melanoma and head and neck cancers.

Another area in which the Radiology Department has contributed enthusiastically to the profile of the Institute has been in teaching. Professor Peter Armstrong, starting from the time of his appointment to Barts in 1989, took the lead. A gifted teacher himself, he taught extensively to undergraduates and postgraduates, introduced imaging as a core module in the Bachelor of Medical Sciences degree in Molecular Medicine. Subsequently, the teaching of cancer imaging was also introduced as a popular module in the MSc in Cancer Therapeutics run by the Institute. With responsibility for undergraduate training held for a few years by Professor Reznek, it was possible to raise the profile and to increase the commitment by the Institute to general cancer teaching.

Modern cancer imaging really started with the introduction of CT. It has been a long and exciting journey from the introduction of the earliest body scanner at Barts in 1980 to the state-of-the-art, 64-detector and 124-detector dual source multidetector CT scanners and a PET-CT scanner within the department today; from the 0.08T MRI to the 3T magnet available alongside a 1.5 Tesla machine. It has allowed imaging to play an increasingly significant role in the management of patients with cancer, and generated a need for a specialist Oncological Radiologist. Such a rapid development has emphasised the need for research into cancer imaging, not only to evaluate the diagnostic performance of the technology, but how it can best be used in the clinical setting. Another ‘first’ was the textbook I co-edited with John Monaghan on Gynaecological Oncology. This was the first such British textbook, with the first edition published in 1985. Within Barts, radiologists, whether academic or clinical, at many levels have

contributed to this process and it is hoped that in so doing has not only promoted the profile of Barts, but also helped clinical colleagues toward more successful management of patients with cancer.

Professor Michael Besser throughout our collaboration in clinical and research work would opine, often in public, "the radiologist's job is to make us clinicians look good"! I often repeat this to younger radiological colleagues when they talk of the glittering success of more illustrious clinicians. Yet the clinical and academic contribution any radiologist can make is greatly dependent on a close working relationship with interested, enthusiastic colleagues. It was my great good fortune while at Barts to have worked with outstanding colleagues and friends.

The Founding of the Barts Cancer Institute in 2004

Ian Hart
Professor Emeritus in Tumour Biology

By late 2002, I had been the Richard Dimbleby Professor of Cancer Research at King's College London for a little over 9 years and professionally I was not happy. The department was located in the Rayne Institute, St Thomas' Hospital, not noted as the epicentre of Biomedical research in London at that time (nor at any other time in fact), and, as a CRUK supported Group which was only one of two in this institute working on cancer, we felt isolated and detached from our peers.

On the positive side, the only major plus was that, in 1998, I had managed to recruit to my department a bright, young 6-year CRUK Fellow who was, I was certain, very much superior to me as a researcher. This individual, Kairbaan Hodivala-Dilke (known to all as 'Kebs') had all the makings of a cancer research 'star' and I was keen, nay desperate, to 'tie her' to me so I could feed vicariously off the academic fame I was sure she would achieve! One of my major concerns was that the professional isolation we all felt would cause Kebs to respond positively to the recruiting overtures I knew she would be getting from other Institutes; loss of her active small group would exacerbate our difficulties. Fortuitously it was at about this time that Professor Sir Nick Wright ("Sir Nick"), who must have known of my disaffection with King's, approached me to determine whether I would be prepared to move to Barts.

Sir Nick had been my line manager ten years earlier when I ran a laboratory in Imperial Cancer Research Fund's (ICRF) Lincolns Inn Fields London Institute and my personal knowledge of his managerial style (non-interventionist and distant!), coupled with the strong support he offered to subordinates, represented an important reason for my desire to discuss with him about possible relocation. He outlined his vision of an expanded cancer focus at Barts with an evangelical zeal which resonated with my wish to rescue my floundering research career. I was sold immediately. Sir Nick had a clear and compelling idea of where he wished to drive the cancer effort at Barts and I thought that this ambition was achievable, not least because he already had outstandingly strong CRUK supported groups within his domain. Andrew

Lister, Bryan Young, Fran Balkwill, Jack Cuzick, Peter Sasieni, and Stephen Duffy all worked on the Barts campus and all were individuals I knew and admired. I was desperately keen to have my laboratory in close proximity to theirs as I knew this could only be beneficial, through greater interaction and abolishing the scientific isolation we had felt so keenly at St Thomas. If we could negotiate a move to Barts no longer would we exist in an environment where Cancer was a poor relation.

Of course, I did not tell Sir Nick of my desperation; even though I wanted to move I still needed to ensure we received a 'good deal' in order to mitigate against the disruption a cross-London move would entail. I did not have a strong hand with which to bargain - I was pushing 55 years of age, my productivity had dropped alarmingly, renewal of my core CRUK Programme Grant in 2005 was by no means certain and, to be blunt, if I was in Sir Nick's position, I was certain I would not be offering the chance he was giving to the likes of me. Why was he proffering me this lifeline? What he'd realised was that Professor Nick Lemoine was similarly unhappy at Hammersmith - he was the real target! Nick and I were friends, with a mutual admiration of our scientific aspirations fashioned by service on the same grant panels, and Sir Nick realised my presence at Barts would be a positive element in his attempts to recruit Lemoine to this locale; I was to be but one worm on the many baited hooks being dangled before Nick's eyes[1].

Discussion with my department, who were kept abreast of these possibilities, confirmed that, irrespective of the reasons behind Sir Nick's plans, they could see only benefits to the potential relocation to Barts (proving, yet again, that old adage that when head of a department, one should employ only those brighter than you!). Importantly, Kebs was happy to accompany me to Barts and we agreed that when she came she would be applying in the next CRUK Quinquennial Review for full P.I. (Principal Investigator) status. All in all, the possibility of working as two interlinked laboratories within the same space was such an attractive one that the acceptance of Sir Nick's offer was the proverbial 'no-brainer'. Thus it was in 2003 that I signed to become Professor of Tumour Biology within Barts and, with the total refurbishment of our laboratory space (largely to the carefully drawn plans of my 'right hand', Dr (now Professor) John Marshall - the ground floor facilities of tumour biology in the John Vane

[1] This abundance of Nicks (some might say overabundance!) means that I will refer to these two protagonists as "Nick" and "Sir Nick".

Building are very much a consequence of the practical knowledge and expertise of John) - we moved into our new facilities as a Laboratory *en masse* in the summer of 2003.

It also was around the time that I arrived that, together with Andrew Lister and Bryan Young, I interviewed a young Chinese cytogeneticist, Dr Yong-Jie Lu, who we recruited as a senior lecturer and team leader to work on prostate cancer. There was no hiding Yong-Jie's deep understanding of cancer genetics and his outstanding publication record. Also, and this is a theme that recurs throughout this chapter, he was evidently a very nice person who would make an excellent colleague. I will return to this facet of the BCI, at least the one that I knew from 2003-2012, but it is worth pointing out at this juncture that I firmly believe one of the reasons for the success of the institute was that it was peopled not just by excellent scientists, but also by folk who were such pleasant individuals that it made working and collaborating together a great pleasure; this type of collegiate atmosphere is essential for the type of rapid and successful development the institute was to undergo.

At the time of my joining the institute, Ian Jacobs, an eminent gynaecological surgeon, was Head of Cancer at Barts, with Fran Balkwill serving as his Deputy. I worked under these two individuals for a period of 9 months and there is little doubt that together they laid much of the vital groundwork for the later successes of the Barts Cancer Institute. However, there was a gifted individual waiting in the wings to serve as a leader. Sir Nick's strategy of bringing in Nick Lemoine as part of his succession planning bore fruit, with Nick signing with Barts in September 2003. Whilst it undoubtedly is true that he built upon the base developed by Ian Jacobs, in my view, and the view of many others, it is the vision and hard work of Nick that from 2004 onwards has propelled BCI to the front rank of UK cancer research institutes. Without the ambition, drive and foresight of Nick Lemoine, it is doubtful that BCI would have reached its full potential.

The intervening 7 months, while Nick's laboratories were being totally renovated, saw the new Head of Cancer (he had not yet had the title of 'Director' conferred upon him) occasionally share my office while he oversaw the development of the lab space for his new Centre and began to plan for the future of the Institute. Although Nick rarely graced my small rabbit-hutch of an office with his physical presence, (his bottom only seemed to touch the reserved chair in my office about twice during this initial phase), through our telephone

interactions and discussions it became clear that our friendship and mutual respect meant we worked well together and, in 2004, he asked me to become Deputy leader of the Institute.

Outside the BCI, with my team following our successful completion of the Wales 3000 Challenge, June 2012;

Left to right, Sab Vallath, myself, Mike Allen, Richard Grose, Alex Pool, Alex Papal and Michalina Gruszka;

We climbed to the top of all 15 mountains over 3000 ft in Wales in 24 hrs - and then went back to work in the afternoon!

The arrival of Nick's laboratory, which became the Centre for Molecular Oncology in May 2004, saw a large increase in the mass of lab bench scientists and clinicians on the Barts site. Professor Helen Hurst and Drs Iain McNeish (now Professor of Gynaecological Cancer, University of Glasgow), Yaohe Wang, Tatjana Crnogorac-Jurcevic and Gunnel Hallden all were persuaded to leave DuCane Road, Hammersmith, for the leafy environs of Charterhouse Square. With the presence of this cadre of gifted researchers, and their teams now functioning in the John Vane Science Centre, one could start to acknowledge the perspicacity of Sir Nick Wright, who had foreseen the boost that recruitment of the Lemoine entourage would provide to cancer research within the Barts environment.

The "leafy environs" of Charterhouse Square

Another addition to the Barts team, also from Hammersmith, was Professor (now the Rt Hon Professor Lord) Ajay Kakkar who in 2004 joined as Centre Lead for Surgical Sciences. It is a fact that this particular Centre never took off, certainly not in the way it was envisaged to have the potential and capacity to develop, and, in my view, this probably was because Ajay's vision and scope were extensive and broad in nature, rather than limited to the more constrained, detailed science that building a functioning centre demands. His "big picture" ambitions were somewhat loftier than Barts could provide for (as illustrated by his elevation to the Peerage and his keynote appointment at UCL in 2011) and he had the need to work on a larger stage. However, this most urbane and charming of clinician scientists was responsible for bringing Mr Bijen Patel, Clinical Senior Lecturer, into the Barts institute and he established our very successful Surgical Sciences MSc, which has contributed hugely to the well-being of cancer patients..

At a slightly more parochial level, though one which would have at least as much impact upon cancer patients as Ajay's teaching innovation, 2004 was also an exciting time for my own Centre for Tumour Biology. John Marshall had started working on breast cancer as a model system to study the role of integrins in modulating the spread of cancers and, as part of this interest, had established a collaboration with a young pathologist at the University of Leicester. After listening to John rave about the energy and knowledge his collaborator brought to their joint studies, I determined that we would be hindered in future developments if we did not have appropriate pathological expertise located within our Centre. With this in mind, I started trying to recruit the young pathologist from Leicester, Dr (now Professor) J Louise Jones. Negotiations reached a successful conclusion and Louise, alongside her small team, joined us in April 2004.

While John had been whispering in one of my ears about the stellar qualities of Louise Jones, Kebs had been whispering in the other about the abilities of someone who had just finished a postdoctoral position with Dr Clive Dickson - a former colleague at the ICRF. This young man, Dr Richard Grose, was not only an excellent scientist well versed in transgenic technology and FGF (Fibroblast Growth Factor) biology, but also a thoroughly nice individual according to Kebs. I always had huge respect for Clive Dickson and knew that anyone trained in his lab would be a more than capable scientist so I met with Richard. As usual, Kebs' opinion was correct and so I set about recruiting Richard Grose as a Lecturer, culminating in his arrival to Head the FGF Signalling Group in May 2004.

Working in Tumour Biology was turning out to be fun; the sparkle was back in being a researcher! As befitted being members of a university department, both Louise and Richard went on to contribute more than just active research programmes. At the time of writing, they also lead on two further successful MSc courses developed and run by the institute, with Louise heading 'Molecular Pathology and Genomics' and Richard (following on from the sterling initial work of Dr Simon Joel) heading 'Cancer Therapeutics'; both courses have brought recognition and kudos, as well as some excellent PhD students, to the BCI.

As 2004 proceeded we made what would turn out to be one of the best appointments we could have made when, in August, Dr Delphine Purves became Institute Manager. My contribution to this seminal decision (I was not involved in the interview process) lay in the serendipitous fact that I'd worked with Delphine before when she was at Elsevier Science and I was Science Editor of the European Journal of Cancer. Delphine had been a huge help while I fumbled my way through learning the publishing trade as a complete amateur and I was able to inform Nick of this helpfulness. Moreover, I re-assured him that, unlike most of my friends, she didn't seem to be a dipsomaniac (a white lie which was soon uncovered when 'champagne' Purves got into her stride at Barts!) A major benefit of this appointment, which was soon apparent, was that now Nick did not have to rely on me, but instead had a professional to act as his 'sounding board' when discussing matters relating to the management of the institute. We now were increasing the effective running of the institute so researchers were less likely to be distracted by the managerial issues; issues which, generally, they had little idea of how to resolve.

2004 segued into 2005 with my enjoyment of working at Barts still increasing exponentially. This enjoyment of the working environment was heightened by a number of appointments made in 2005. Firstly, during this year we were fortunate to persuade Professor John Gribben, one of Harvard's luminaries, to return to the UK and take up a post as designate Lead for Haemato-Oncology (anticipated to be upon Andrew Lister's retirement rather than his demise, we should reassure Andrew at this point). John's arrival was a considerable coup for Barts and ensured the continuing commitment to outstanding translational work from bench to bedside in Haemato-Oncology that Andrew and his team had pioneered. Dr (later Professor) Norbert Avril was recruited from the University of Pittsburgh to develop a PET (Positron emission tomography)

oncology programme within the Centre for Molecular Oncology, and this had the added benefit of bringing Professor Steve Mather and his team, including Dr Jane Sosabowski, over from the Nuclear Medicine Department within the hospital to the Charterhouse Square site. A consequence of this relocation was that pre-clinical molecular imaging, an increasingly important component of many of our biological studies, was raised to highly competitive international standards and this has had a major positive impact on the quality of publications arising during the development of novel therapeutics, such as antibodies and oncolytic viruses, which are close to entering clinical trial.

In February 2005, Tumour Biology was fortunate to welcome Mr (now Professor) Hemant Kocher as a Senior Clinical Lecturer, and hepato-biliary-pancreatic surgeon, who came to us on a National Clinician Scientist Fellowship. Hemant is a rare bird indeed; not only a gifted surgeon working in a complex specialization, but also a true scientist with an excellent knowledge of cellular biology, statistics and molecular biology. His desire to understand at the cellular/molecular level how communications between cell populations affect pathogenesis of pancreatic cancer already has paid dividends in patient benefit, as he starts to take novel treatments into clinical trial. Additionally, Hemant serves as a superb role model for young surgeons to show them how a busy clinical career need not be a hindrance to a similarly sparkling academic career. Only a month or so later another young scientist and French émigré (why hasn't the scientific community been more vociferous lately in pointing out just how much British academia has benefitted from immigration?) joined our Centre as a lecturer. Stephanie Kermorgant came to us from Peter Parker's lab, where she had developed the concept of spatio-temporal intracellular signalling, an important refinement to the prevailing view of the regulatory biochemical pathways, which modulate both normal and transformed cell behaviour. Stephanie's group has made major strides in documenting the importance of this phenomenon and, perhaps more importantly, how disruption of spatial signal localisation can affect tumorigenicity and metastatic proficiency.

After this recruitment, the institute settled down somewhat to work toward what we knew would be the incredibly important Research Assessment Exercise which would occur in 2008, an event which would either make or break us as a viable player on the 'cancer research stage'. In 2006, an opportunity presented itself to consolidate our emerging status as a world-class research institute and to position ourselves even more strongly for the upcoming RAE. We became aware that the Ludwig Institute for Cancer Research at UCL would

be moving to Oxford and that not all the Group Leaders necessarily would be amenable to such a relocation. Accordingly, Bart Vanhaesebroeck was 'targeted' as our next possible acquisition, with Nick Lemoine and myself wooing him assiduously. My role was to act as his drinking partner over several recruiting dinners; as they say, 'a tough job but someone has to do it'. Bart, who even at this stage in his career was an eminent scientist and world leader in cell signalling, had a specific interest in the PI-3 kinases and had made major contributions including the discovery of the p110delta isoform and understanding its role in B-lymphocyte signalling. Luckily, our courtship of Bart resulted in 'marriage' and in 2007 he became the lead of the Centre for Cell Signalling, where he would remain until 2014. Bart brought with him a number of publications in first-rank journals, which we knew would bolster our nascent RAE portfolio; good to know that all the headaches I had suffered after our recruiting meals were for the greater good of the institute. Just as important for our institute as this dowry of outstanding manuscripts that Bart Vanhaesebroeck brought with him was the fact he also brought with him Dr Pedro Cutillas, an expert in proteomics under whose co-supervision, with Dr Simon Joel, a most valuable mass-spectrometry facility was established in the John Vane building.

I don't think it is an overstatement to say that the RAE results published in 2008 were a triumph for our developing institute. In cancer we were ranked 3rd out of 14 submissions in terms of 3* and 4* outputs (international quality) and we were joint 5th overall (gratifyingly beating the traditional big three in London - King's, Imperial and University College London - as well as powerhouses such as Oxford) throughout the UK. These remarkable achievements were so gratifying, both for the old-timers and for new recruits, that we would have celebrated for years and extended our self-congratulatory partying indefinitely had not something appeared on the horizon almost immediately that required us to look forward, not back at past successes, as a means of getting the institute to where it should be. In late 2008, Cancer Research UK published their strategy for 2009-2014 in which they announced the intention to establish a UK wide network of up to 20 CRUK Centres, which would benefit from sustained infrastructure and training support. If for no other reason than that CRUK Training Fellowships for younger clinicians would be restricted to such Centres of Excellence, it was essential that Barts, with its outstanding record of training clinician scientists under Andrew Lister's regime, was part of this designated network. At the very minimum, the kudos gained from our strong showing in the RAE would stand us in good stead as we prepared our submission. The relative opacity of CRUK's guidelines however meant that Nick, Delphine and

I still felt very much in the dark as to what exactly 'they' wanted when we put the application document together. Not until the final announcement, when we became the first CRUK Centre in London and one of the first in the UK, did we feel truly confident of the outcome.

A major positive aspect of preparing the submission was that Centre status was requested, and granted, on the basis of including a considerable amount of population and early detection studies in our portfolio. This was predicated upon the involvement of our epidemiology colleagues who, within the university, remained sequestered in the Wolfson Institute. Sharing membership of the same CRUK Centre of Excellence with Professors Cuzick, Duffy and Sasieni has led to an expansion in the quality of work involving collaborations (and even more substantial interactions such as the location of Dr (now Professor) Dan Berney within the Centre for Molecular Oncology) which augurs well for the forthcoming period of Centre membership. In 2014, under the leadership of Nick Lemoine and Kebs Hodivala-Dilke, continued membership of this network was awarded in the face of even tougher competition for a reduced number of CRUK Centres; recognition of the impressive quality of the work conducted in the first 5 years of CRUK sponsorship.

While the 2009 CRUK recognition of the institute seemed to be setting cancer research at Barts on course for further future success, there was one potential difficulty on the horizon; as with so many perceived problems, this one also offered as many possibilities as it offered difficulties. The predicament was that several of the senior scientists were a bit too senior. It would be hyperbole to claim that getting into the Boardroom for various meetings necessitated climbing over a mass of assembled Zimmer frames, but there was little doubt that we needed to embark on a plan to ensure that, when the generation who found themselves next on the diving board finally took the plunge, there were younger investigators who could take over. Between 2007 and 2012 (when this author quit the fun of working in the BCI and finally accepted that he was now well and truly edging along on the diving board), there was a whole slew of appointments.

Wonderfully, most of the appointments we made during this period have turned out to be great successes. Whether this is a consequence of the astute insight of the interviewing panels, the magnificent opportunities presented within the Barts site or, as I suspect, the sheer quality of our young investigators, is uncertain. Thus within this period we appointed Dr (now Professor) Tom

Powles, in 2007, Dr Claude Chelala was employed as lecturer in Bioinformatics in 2006; Dr Peter Szlosarek, following a successful Postdoc period in Fran Balkwill's Centre for Cancer and Inflammation, became clinical lecturer in 2008; Dr Li Jia moved from the Blizard Institute to the post of non-clinical senior lecturer in Haemato-Oncology in September 2008; Dr Michelle Lockley, who had done her MRC-funded PhD with Nick Lemoine and Iain McNeish, returned as senior clinical lecturer in 2009; Dr Tyson Sharp arrived as a Lecturer in Molecular Oncology in 2012, becoming Centre Lead in 2015; Dr Jeff Davies was persuaded to leave Harvard and take up appointment as clinical senior Lecturer in 2011; Dr Melania Capasso was appointed in April 2010 as lecturer in Cancer and Inflammation; Dr Sarah Martin was appointed lecturer in September 2010. Quite a roll-call of young talent, with huge potential for the future, though their contributions have already been immense.

Staff & Students entering Charterhouse Square, home of the BCI

The Future

When I retired I made the 'boast' at my retirement lecture that during my tenure as Centre Lead, my beloved Tumour Biology had published, over the 8 years of my time at Barts, a minimum of 103 publications with an average Impact Factor of 8.2. I was immensely proud of this figure, which represents a large numerical output of high quality manuscripts. Checking lately I notice that, since my departure, this average IF actually has increased; it is a sad blow to my idea that I was indispensable since, in my absence, Tumour Biology staff have been publishing better papers in better journals. Luckily, one thing I did learn from working with my epidemiology colleagues is that association does not (necessarily) imply causation! Had I wished to have claimed some credit for the whole institute at my retirement, I am sure the calculated figures would have been equally good (probably better, given that colleagues who headed other centres, such as Fran Balkwill, soon did the calculations and were keen to point out that their metrics were even better than mine!) Whatever the numbers, I am sure they show the same surge, post my retirement, as that seen in the Centre for Tumour Biology. This is easier (and is less damaging to my ego than the reasons others will have come up with) to explain.

The explanation is that the quality of the personnel, and the quality of their output, keeps increasing. Since I have left, Nick Wright has taken over as Centre Lead of Tumour Biology (a major promotion after his tenure as Warden of the entire Medical School), Professor Chris Heeschen has established the Centre for Stem Cells in Cancer and Ageing, Professor Peter Schmid now is Lead of Experimental Cancer Medicine, Andrejs Ivanov and Sergey Krysov have become Lecturers in Haemato-Oncology; Rifca Le Dieu now is Clinical Senior Lecturer in the same Centre, Stuart McDonald is a Lecturer in Tumour Biology, Patricia Sancho is Lecturer and Alexander Aicher senior lecturer in Cancer and Ageing and Bela Wrench also is a Clinical Senior Lecturer in Haemato-Oncology. Even more excitingly, we have several Early Career Lecturers - Katiuscia Bianchi, Angus Cameron, Esther Castellano-Sanchez, Gabriella Ficz, Susana Godhino, Trevor Graham, Sarah McClelland and Paulo Ribeiro. If I wasn't so comfortable doing nothing in my rural idyll I could salivate at the thought of the opportunity of returning to work with these young investigators. It is inevitable, given the attrition rate associated with academic careers, that not all of these individuals will thrive at Barts but, and it is a very big but, they are so good that all of them are bound to thrive somewhere. Thus, while they are struggling to consolidate their academic reputations, the major beneficiary will be the BCI, an institute which has faith in young investigators and has recruited some real stars. I can only see this Institute becoming stronger over the next 5-

10 years and, with its focus upon translating findings for patient benefit, this will be vital given the Crick Institute offers such a competitive strong focus for basic biomedical research in London. The major successes listed below are based very firmly upon the considerable impact BCI has had on cancer patients and my sincerest wish is that such impacts will continue to be made over the next decade.

Major Achievements since 2004

It is a remarkable testament to the quality of my former colleagues that the only difficulty I face here is that there is an embarrassment of riches; an embarrassment which I must pare down to a manageable level. I have been highly selective in making my choices. Let me apologise upfront to those whose specific work and contributions I fail to acknowledge in this section; it doesn't mean I am unaware of their work nor that I fail to appreciate the quality of what they have achieved. It just means I am constrained by space limitations from listing every single achievement in the last ten years. Accordingly this is a personal view and one based very much upon subjective assessment; opinions will vary as to what should be on this list but, as I am the one actually doing the typing, this is not for debate! This is my view of the major achievements at Barts Cancer Institute[2].

- The RAE of 2008. At the time this truly rocked the established order in the cancer research firmament and let UK oncological science know that Barts was now a major force to be reckoned with in the cancer field. The fact that there was a resurgent Barts in other disciplines also meant that, as part of an integrated Medical School, we were seen as being highly competitive at the major funding agencies. While the REF results of 2014 are rather more opaque *vis-à-vis* cancer, because of our embedment within Clinical Medicine, it seems that ground was not lost. Impact in breast cancer and preventive measures in cancer was singled out for particular praise. These two National evaluations must count as substantial achievements by the Director and his team.

- Installation of BCI as a major component of the CR-UK Centre of Excellence in 2009 coupled with the even-more-difficult to achieve re-validation in 2014. This recognition, essential to access so many funding streams from the

[2] Note also the limitation to BCI which precludes me from listing the seminal contributions from CRUK Centre colleagues in the Centre for Cancer Prevention, located in the Wolfson Institute

major supporter of UK cancer research, is testament to the hard work of Nick Lemoine, Kebs Hodivala-Dilke, Delphine Purves and their teams.

- Achieving acceptance from an initially obtuse and obstructive college that the name "Barts Cancer Institute" was the only sensible option for our identification since it carried brand recognition both nationally and internationally. The identity this conferred on our institute was achieved only after a hard-fought campaign by both Nick and Sir Nick.

- Acquisition and renewals of CRUK Programme Grants are no longer the 'be all and end all' they once were and we have to accept that, in future, fewer P.I.s will hold these grants (not such a problem as long as CRUK Centre status is maintained). Nonetheless the gaining and holding of these important grants is a considerable achievement and, since 2004, Nick Wright, Nick Lemoine, Kebs Hodivala-Dilke, Andrew Lister, Bryan Young, Jude Fitzgibbon, Bart Vanhaesebroeck, Fran Balkwill and myself have all either obtained or renewed their Programme grants.

- Award of European Research Council grant to Fran Balkwill for her 'CanBuild' initiative.

- Creation of the Tissue Banks held at Barts. Perhaps it was the example of Andrew Lister and his team who were years ahead of everyone else with their fastidious storage of clinical material linked to detailed clinical data but, for whatever reason, Barts must be the premier institute in Britain for obtaining and retaining high-quality patient tissue. Moreover, although academic pathologists are a rare breed, we are fortunate to have two in control of these vital repositories. Thus Louise Jones, supported by a large core grant from Breast Cancer Campaign, is the Principal Investigator for a Breast Cancer Tissue Bank, which together incorporates the novel and exciting isolation and storage of the different cell populations that comprise the various identified molecular sub-types of breast cancer. Dan Berney heads the Genito-Urinary Tissue Bank, supported by the generosity of Orchid, which archives male-specific tumours. These samples have provided colleagues, in the Wolfson particularly, with valuable resources to underpin their epidemiological investigations. Female-specific cancers are similarly catered for by the Gynaecological Oncology Tissue Bank under the lead of Michelle Lockley. The bank contains tissue from both primary and metastatic disease. Rather more recent, but particularly strong on the numbers of included cases of mesothelioma, is the Lung and Mesothelioma

Tissue Bank headed by Peter Szlosarek. Under the Leadership of John Gribben, the Haemato-Oncology Tissue Bank, so valuable in the past, continues to expand. A recent exciting expansion of these existent banks is the on-stream development of a Barts Metastatic Tissue Bank (joint leadership of Louise Jones and Hemant Kocher) focusing on Hepato-Pancreato-Biliary, Breast, Lung and Gynaecological cancers. Finally, the latest addition is the National Pancreatic Tissue bank, starting in 2015, for which Hemant Kocher is the lead.

- The sheer endurance and commitment of John Marshall in taking $\alpha v\beta 6$ peptides and antibodies (264RAD) through pre-clinical evaluations right to the very threshold of clinical evaluation.

- The similar tenacity exhibited by Yaohe Wang in analysing the efficacy of replication-selective oncolytic viruses and creating a body of work which will lead to their more efficient use in the clinic.

- The clever and exciting use of transgenic mice, to dissect out the role of adhesion receptors and their associated molecules in angiogenesis, by Kebs Hodivala-Dilke. This has culminated in two seminal papers in the past year which have been paradigm-shifting in affecting the way we view tumour vascularity as a potential target for therapeutic intervention. These studies showed (i) that targeting endothelial cell FAK (Focal Adhesion Kinase) sensitises tumours to DNA-damaging therapy and (ii) that actually enhancing angiogenesis can reduce tumour growth and spread, when it is combined with chemotherapy.

- Tom Powles' demonstration that anti-PD-L1 treatment has clinical activity in metastatic bladder cancer, the first major advance in the treatment of these malignancies in the past 30 years.

- Work from Fran Balkwill's centre showing cytokines, and particularly Interleukin-6, are *bona fide* targets for anti-cancer therapy in human ovarian cancer.

- Recruitment of so many outstanding young investigators; this is not an Institute which is allowing itself to fossilise.

Lack of remaining space prevents me from continuing along the track of

documenting where and how these and other Barts-based translational research efforts have resulted in direct patient benefits (either immediately or in the immediate future), which must be an indication of the strengths and achievements of this only ten-year old institute. What the basic scientist in me insists should also be known is that these works, and other more fundamental studies, have not in any way been at the expense of quality publications. Thus, if we take from 2007 onwards, a time when the institute was just getting into its stride, we find, amongst the more 'bread and butter' papers in *Cancer Res*, *Oncogene, J Path* etc. senior author papers (i.e. ignoring similar outputs where Barts authors might have been invaluable contributors) in such premiere journals as *J Clin. Invest.* (Hodivala-Dilke, Gribben, Lemoine, McNeish), *EMBO J* (Hurst, Grose), *Nature* (Godinho, Hodivala-Dilke, Powles, Vanhaesebroeck, Hodivala-Dilke), *Nature Cell Biol.* (Kermorgant), *Proc Natl Acad Sci* (Balkwill, Capasso, Cutillas, Gribben), *Gastroenterology* (Heeschen, Kocher, Kocher), *J Cell Biol* (Grose), *Nature Genetics* (Fitzgibbon) *Nature Immunology* (Vanhaesebroeck), *Sci Signal* (Cutillas), J *Natl Cancer Inst* (Marshall), *Cancer Cell* (Hodivala-Dilke). This works out at over 3 papers per year in the very top-ranked journals; an excellent rate for any comparably sized university institute.

My retirement dinner, from left to right, Louise Jones, Katie Goodey, Nick Thatcher, Jean Mossman, myself and Francis ("Mrs H") and John Marshall, December 2012

Impressive as these dry facts are, when I come to look back on my eight years at Barts, what I actually feel was the biggest achievement of all of the Institute

is the sheer fun of working there which it managed to engender. If Mr Charles Dickens were writing this chapter he might well have summarised by saying "What larks, Pip, what larks" (*Great Expectations*). The colleagues I had were terrific to work with, but also great to socialise with too. To have had this much fun yet, hopefully, have contributed something to the reputation of this terrific institute is something I hope others can, and will, taste over the next decade.

Special Contribution
The History of Radiotherapy at Barts

Nick Plowman
Lead Consultant, Head of Radiotherapy
Bart Health NHS Trust

Within a remarkably short space of time following the discoveries of Xrays (Rontgen 1895) and radium (the Curies 1898), Xray/Radium departments of diagnostic and therapeutic radiology existed in major European hospitals, including Barts.

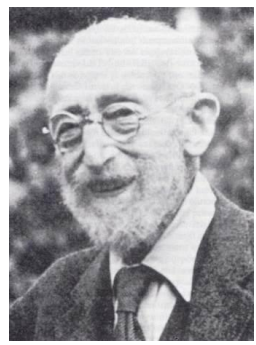
Xrays and radium surface applicators were in use for the treatment of superficial cancers from the beginning of the 20th century but it was not until 1919 that an organised investigation into their application and effects was scientifically drawn together by a specially appointed 'Radium Committee' within St Bartholomew's. In that year, a quantity of radium, which had been used in gun-sights in the Great War was given by the Government to Barts. From the outset, the Radium Committee initiated and supported research and the organisation of a Radiotherapy service. In 1921, following a visit of some of that committee to Erlangen the new 200 kV "deep Xray" apparatus was purchased and the formal radiotherapy service established. In 1928, at the second International Congress of Radiology in Stockholm, the internationally accepted unit of radiation exposure the rontgen (later the Rontgen) was accepted and credible radiotherapy commenced.

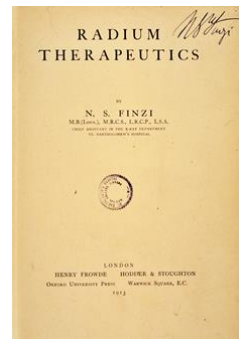
Patient being treated by radiotherapy for breast cancer, around 1900, at the London

Patient being treated with radiotherapy around 1900. Photograph courtesy of St Bartholomew's Hospital Archives (Ref: X8/1658)

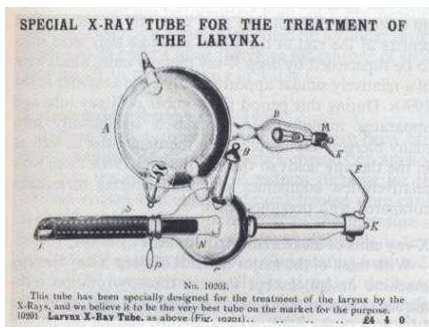
Ronald Canti (pictured; whose son, Gordon, was the head of the Department of Cytology at the hospital up until 1990 – establishing the role of cytological diagnosis in Oncology) demonstrated, by phase lapse cinematography, the lethal effects of radium ionising radiation on cancer cells and went on to become honorary secretary of the Barts' Cancer research committee in the 1920's (more of this below).

In 1912, Dr Neville Finzi was appointed as the Director of the Xray department at Barts and together with other keen colleagues (amongst whom Ronald Canti was important) he attracted funds such that, in 1924, Barts was able to set up the "Radiotherapeutic Research Department" – one of the, if not the, first such Radiotherapy Department in the world. His published work: Radium Therapeutics led the subject in that era.





Neville Finzi – in the flush of youth and in maturity; and the cover of his masterpiece, "*Radium Therapeutics*"



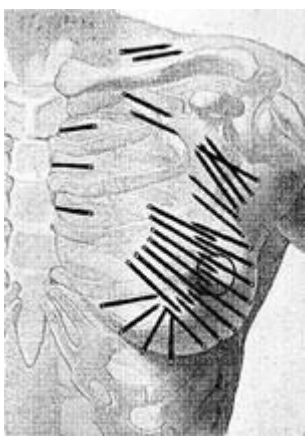
The Finzi-Harmer fenestration technique for radium therapy of laryngeal cancer was a world first and proved successful in this cancer, for which localised radiotherapy remains the gold standard for cure with organ preservation.

Figure of Finzi-Harmer radiotherapy technique for larynx cancer

Sir Geoffrey Keynes (pictured front cover) was the younger brother of the celebrated economist, John Maynard Keynes. He combined his surgeon's career at St Bartholomew's Hospital with the publication of bibliographies - such as those of the poet, John Donne, and the scientist Robert Hooke - much respected by the bibliographic and literary worlds.

Keynes completed his MD in 1918 and the Final FRCS in 1920 when he was appointed as first assistant to the new professorial unit under the whole-time directorship of George Gask. Keynes observed that radical breast operations were not curing patients. Gask encouraged him to investigate the use of the then newly acquired radium for the treatment of locally recurrent disease. Keynes inserted special needles made of radioactive radium into the breast and even into axillary lymph nodes to sterilize the cancer.

So impressed was Keynes with the results that he extended the treatment from patients with advanced primary cancer to those with operable disease, for he was gravely dissatisfied with the results of radical surgery which he shortly abandoned. In a succession of papers between 1927 and 1937 he recorded his experience with conservative surgery and irradiation His full results were published in the British Medical Journal in 1938. He was full surgeon at the Hospital between 1946 and 1949, and, in addition to the breast cancer work he helped to develop an effective blood transfusion service and to advance surgical treatment of thyroid disease. During World War Two he was senior consultant surgeon to the Royal Air Force. His own library is now in the Library of the University of Cambridge.



D**r. Keynes's technique of inserting radium needles into the breast for the treatment of cancer**

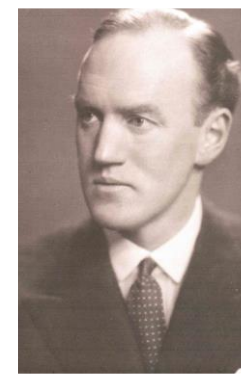
The Keynes technique for interstitial Radium brachytherapy for early breast cancer was also a world first and, although becoming eclipsed for several decades by the later (reworked radical surgical) Halsteadian thesis that extensive surgery was needed to cure this malignancy, nevertheless, with the passage of time, Keynes brachytherapy work has come right back into mainstream therapy – in that wide local excision and radiotherapy to the breast is now considered as optimal therapy for selected patients – this started at Barts.

Head of Radiation Physics from 1920-1950 was **Professor F L Hopwood** (pictured) – a giant in the field of Radiation Physics and very important in the development of Megavoltage radiotherapy.

In this period, forward thinking in many radiotherapeutic fields was pioneered at Barts – one example being Finzi's suggestion that – for Hodgkin's disease, that the radiation therapy portals should extend to the next echelon of lymph nodes. In the 1970's, at Stanford, California and under the aegis of Henry Kaplan, this extended field methodology for Hodgkin's Disease was furthered with the Mantle and Inverted 'Y' techniques, which became the standard way to cure stage 1-2 Hodgkin's disease for several decades. The concept was born at Barts.

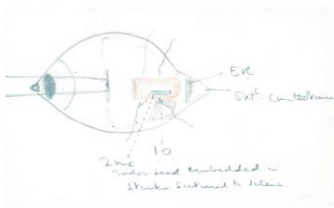
Historically, and in addition to the work of Keynes, radiation brachytherapy has had firm historic roots in the hospital. In 1929 at St Bartholomew's, Foster Moore (I929) first demonstrated that radiation therapy could destroy ocular retinoblastoma, Foster Moore's radon seeds were sutured over the retinoblastoma using ophthalmoscopic localisation. The very high doses of radiation used by these earlier workers frequently caused severe complications, sometimes leading to the loss of the eye.

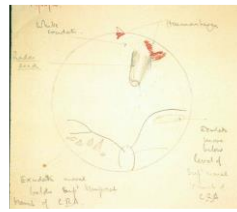
From a study of the histological sections of eyes treated with radon seeds at Barts by Moore, Stallard, and Milner (1931) determined that a dose of 3,500r was lethal to retinoblastoma cells – an important and one of the first dose effect studies in radiotherapy.



Hyla Bristow "Henry" Stallard (adjacent photograph; 28 April 1901 – 21 October 1973) was educated at Gonville and Caius College, Cambridge, where he studied medicine. At Caius, he was a contemporary of Harold Abrahams, and a member of the University Athletics team in 1920, 1921 and 1922. Stallard competed for Great Britain in the 1924 Summer Olympics held in Paris, winning the bronze medal in the 1500 metres and finishing fourth in the 800 metres. He was portrayed by Daniel Gerroll in the 1981 Oscar-winning film: *Chariots of Fire*. Stallard went on to have a distinguished medical career. As Ophthalmic Surgeon to St Bartholomew's Hospital and Moorfields

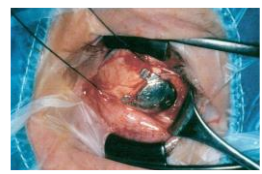
Eye Hospital, he pioneered cobalt plaque radiotherapy for the treatment of ocular tumours, particularly in children. In collaboration with George Innes from the Radiotherapy department at the hospital, they led to the development of Cobalt-6o applicators/plaques, sewn onto the sclera over the tumour. These came in varying sizes and could deliver a dose of 4,000r to the summit of the tumour in 7 days.





Stallard's drawings of the original radium plaque, (courtesy of Mr J L Hungerford)

Their subsequent use has largely been in the therapy of ocular melanoma and derivative plaques (safer for the operator to handle have now replaced the cobalt 6- plaques – iridium isotope plaques now being favoured). This practice was still ongoing at the Hospital until April 2015 when dark forces pulled all the famous ophthlamic oncology services into Moorfields and it is likely that the famous history of Barts Ocular Oncology will be lost – except to the cognoscenti.



An ocular plaque in current service

By 1930, the Xray therapy department was housed on the fourth floor of the outpatient block and had an inventory of two non-shock proof, partly protected 200 kV d.c. units, which in order to maintain serviceability, were usually run at 180 kV. Appositional fields were manually placed on superficial tumours, as there was no sophisticated planning in those early days.

In the units, the tubes and rectifiers were sealed off. It was very difficult to remove all the gas from metal and glass parts. Sooner or later a little gas would be evolved and, despite getters, a gas discharge would take place, often generating a high voltage surge, resulting in an external 'flash' over the unit, sometimes with puncture of the envelope. Further, if the gas discharge persisted, the metal surfaces were roughened, producing a high potential gradient part with internal flashing-over of the unit and its destruction – such were the problems for the Radiotherapy Department in those early days. When treating a patient, in order to reduce the whole body dose, due to poor

protection of the tube, an area surrounding the treatment field was covered with lead rubber. If the HT ends of the tube were close to the patient, this lead rubber was extended over this part of the patient and, being solidly earthed, gave shock-proof protection to the patient. In addition to these technical problems there was the overwhelming problem of poor deep penetration of the beam. The half value layer of 200 kV beams being 3-4 cm only, it was necessary to apply a very high surface dose to the skin in order to deliver any significant dose to the deep seated tumours – severe skin reactions were a part of early orthovoltage radiotherapy. Nevertheless, good therapy treatments occurred in those early days, particularly for superficial cancers. The concept of using several cross-firing fields was born in those early days, thereby sparing the skin dose (by sharing skin exposure over a larger area).

Early radiotherapy equipment in clinical use at Barts. Image courtesy of St Bartholomew's Hospital archives (Ref: SBHX8/180)

The desire for higher voltage equipment that could deliver more penetrating beams of radiation (a desire that was partially accomplished by the radium, isotope derived beams) was at the forefront of the minds of the physicists and clinicians at Barts and, as early as 1927, Dr Edward Allibone constructed a continuously evacuated tube for 400 kV xrays and, in Cambridge, Cockroft and Walton had, in 1932, constructed a tube and generator for 600 kV – having two stages of acceleration.

In 1933, Edward Allibone (pictured) and his associates at Metropolitan Vickers were confident that a tube of similar design could be built for voltages up to 1000 kV. The Cancer Research Committee at Barts were propositioned by Finzi and Hopwood and shared their enthusiasm, but , then as now, the financial aspects of the proposed project were daunting.

Finzi gave the 1933 Mackenzie Davidson Lecture to the British Institute of Radiology on: 'Xray and Radium therapy of the future' and floated the concept of a Megavoltage xray era at this time by concluding that the advantages of developing photon/Xray beam radiotherapy of similar energy as radium gamma radiation would hold enormous promise for the future of Radiotherapy as a clinical discipline. He said: "it seems likely that the future will depend on the ability of the manufacturers to construct a tube working at 1-1.2 million volts, and if the earthed tube Metropolitan Vickers can be constructed to work at these voltages it seems to possess insuperable advantages…..Perhaps I am taking on too much for granted in assuming that some relatively well-off person – and such a benefactor for radiotherapy is badly wanted – may be found to put down the money for the initial apparatus and its housing and maintenance, and that a research worker would be appointed to use it of ……. its possibilities…."

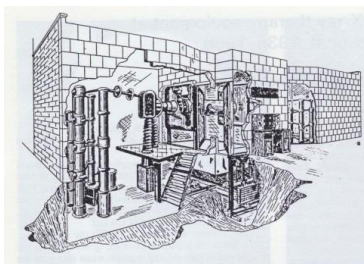
Within two months, Ronald Canti's office received an overture from Mrs Meyer Sassoon that she would be interested in being the sponsor that Finzi had wished, ultimately funding both the equipment and the building. By this time, the Barts' Cancer Research Committee was chaired by Lord Horder and through his influence the Governors of the Hospital allowed the venture to be sited at the end of the Square – a site about to be vacated by two operating theatres. There was a codicil to the agreement that the rare variety of black poplar tree, growing peacefully at this corner of the square, was not to be disturbed. The Sir Halley Stewart Fund came up with the stipend for the Research fellow and Ralph Phillips (an experienced physicist) was appointed to the Megavoltage project for a five year term. Metropolitan Vickers obtained the contract to build the machine.

The building and installation of the equipment was no easy task. The tube itself was 30 feet long and weighed ten tons and had to be accommodated in that corner space of the Square at Barts. George Innes joined the team as a second physicist – temporarily – but stayed for the next 30 years! - later to become Chief Physicist. Whilst the conception of the megavoltage machine at Barts was due to the indefatigable work of Finzi, Allibone and Canti, the commissioning of the

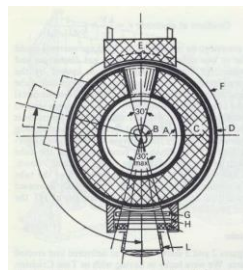
machine into clinical service was due to the hard work of Phillips and Innes. The technical aspects of the installation have been reviewed by George Innes (Brit J Radiol 1987; suppl. 22 pages 11-16).

The diagram below shows a high-voltage anode/cathode assembly supported by glass insulating rods. The electrons produce X-rays per conventional method by hitting the opposed wedge. The X-rays were produced in the middle and emerged from the centre end. It is believed this is why there is this graduated layer of "blocks" around that area. The wheel presumably was a control to set the accelerating potential.

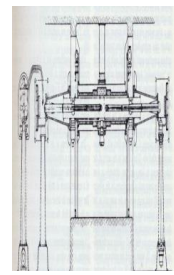
The line drawings of the 1 Megavolt machine



Housing of the 1 MV apparatus



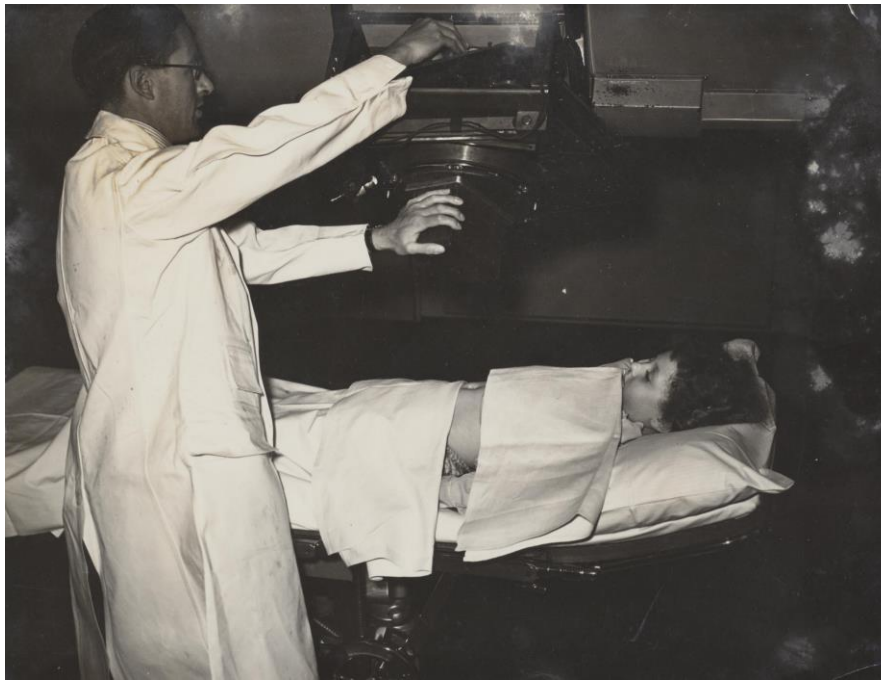
Cross-section, 1 MV X-ray therapy tube



Longitudinal Figure

"The Mozelle Sassoon Department" at Barts was opened by Mrs Meyer Sassooon on December 10th 1936 in a ceremony attended by many dignitaries including Lord Rutherford. The apparatus proved absolutely reliable in action, the Xray output varying by less than 1%. The great gain in depth dose (compared to 200kV) was especially apparent for small field sizes (e.g. a 100% gain at 15 cm for a 6x4 cm field/portal). From 1939, full isodosimetry was produced for individual patients being treated with 1 MV Xrays – another first for Barts Radiotherapy.

Ralph Phillips wrote in 1939: "The installation of the 1,000,000 volt Xray tube at Barts may well mark an important step forward in the campaign against cancer" – how true his words have proved.



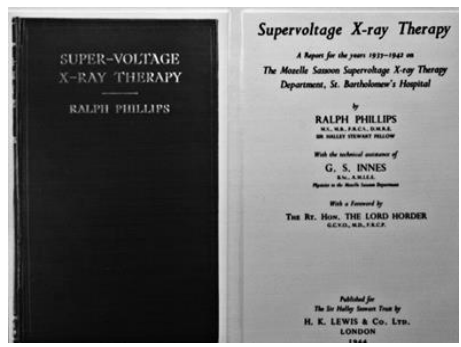
Dr Ralph Philips treating a child, 1939. Image courtesy of St Bartholomew's Hospital Archives (Ref: RD/2/2/10).

The Second World War broke after this and the machine had its fair share of excitement: In his 1944 annual report, Ralph Phillips wrote: "The apparatus has given five years of uninterrupted service. Its running has occasionally been interrupted for a day or two after some of the heavier air raids on London, owing to failure of water and electricity supplies but the Department has been fortunate in escaping damage, particularly when a 750 lb bomb fell only ten yards from the Department – but failed to explode." Ralph Phillips was subsequently poached by Sloan Kettering Memorial Hospital in New York to bring Megavoltage Radiotherapy to the USA.

The 1 MV X-ray Machine

Construction of the enormous 1,000,000 volt X-ray tube in 1939. Images courtesy of St Bartholomew's Hospital Archives (Ref: RD/2/2/6)

One end of the X-ray tube in the Mozelle Sassoon department



Ralph Philips and his famous treatise on supervoltage radiotherapy

The clinical work on the MV apparatus demonstrated the physical advantages of the higher energy beams: increased penetration (better depth doses), better beam collimation (less side scatter – with less collateral dose to adjacent tissues), relatively uniform dose deposition throughout all tissues, from bone to all soft tissues (as Compton absorption takes over from photoelectric absorption at Megavoltage range), and the skin sparing effects of the 'build-up' phenomenon (where the flux of secondary electrons takes a depth to reach maximum beyond an air-tissue interface), together with a high Xray flux (permitting treatment at distance) all were major advantages. The team demonstrated differences in radiobiological equivalence (RBE) of orthovoltage and megavoltage Xray therapy with regard to efficacy of cell-kill – vide infra.

In a series of publications over the next 15 years, the staff of the Barts team demonstrated these advantages in the therapy of patients with cancers of the antrum, cervix uteri, rectum and brain tumours, as well as other rarer tumours – e.g. thymic tumours and glomus jugulare tumours. The improved skin sparing/better depth doses and the integral doses and the optimised individual planning were some of the most noteworthy.

Prof. Arthur Jones

Arthur Edward Jones (pictured), was born 1st February 1919 in Denbighshire, Wales, educated at Grove Park School Wrexham and the Barts Hospital (1937-1943), where he was awarded three scholarships and an exhibition. He served in the army during the second World War and became the specialist neurologist in charge of the Army's Hamburg Unit, with a particular expertise in head injury care (having trained in this period under the famous neurologist: Sir Charles Symonds). After the war, Jones rose rapidly through the ranks at Barts and entered the Radiotherapy Department, where he became a Consultant at the age of thirty and deputy director at the age of 41 in 1950.

As a consequence of his neurological training, Jones became interested in the tolerance of the central nervous system to radiation. His meticulous care in the planning and execution of megavoltage radiotherapy made him an international authority during this time and he led the Radiotherapy Department at Barts for some thirty years, consolidating and extending safe and curative megavoltage radiotherapy. His 1948 publication on: "Clinical reactions and injuries in Supervoltage Radiotherapy." (Proc. Roy. Soc. Med: 1948; 41: 703)

is a good example of his careful observations. His published data on therapy results for many tumours – the thymic neoplasm mentioned above, thyroid eye disease and the optimal therapy of pituitary tumours all attest to his highly significant contribution to modern radiotherapy. His original description of Lhermitte's sign, occurring as a subacute reaction following cervical spine radiotherapy is typical of his careful attention to every detail of radiotherapy practice (Brit J Radiol. 1964; 37: 727).

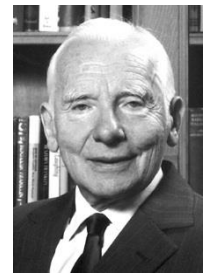
In 1960, Jones was given the rare honour for a non-surgeon of becoming the Hunterian Professor at the Royal College of Surgeons, in 1963 he won the Roentgen Medal of the British Institute of radiology and1978 he was awarded the Royal College of Radiologists' Glynn Evans medal.

During this period and on a level with the Lhermitte's sign observation, John Freeman, who was undertaking all the radiotherapy of children form Great Ormond Street, as a consultant in the Barts' Department, made another interesting neurological observation in children having prophylactic brain radiotherapy (following achievement of remission of acute lymphoblastic leukaemia) – viz the development of a transient period of 'sleepiness' a month or so after finishing the a radiotherapy – the so-called: 'Somnolence syndrome'. Freeman first published this observation in the 1975 British Medical Journal. This was another subacute post-radiotherapy reaction on the nervous system described first locally here at Barts.

Professor Jones was the UK and USA Government advisor for the possible adoption of Neutron Beam radiotherapy, when, in the 1980's, this seemed to have promise. (The author remembers being Jones' Senior Registrar when the professor was called to the USA to a Senate Neutron meeting; from Heathrow, I was called to alter by a single fraction the prescription of a patient undergoing therapy in the Department for a rodent ulcer – so meticulous a leader we had at that time). The overall conclusion was that Neutron beam radiotherapy had more limitations than advantages. However, subsequent interest in particle beam radiotherapy has developed in Proton beam radiotherapy, a particle based radiation therapy method that carries with it the Bragg peak phenomenon – vide infra.

In 1950, Barts decided on the newest Vickers 15 MV linear accelerator to maintain its world lead in the field. There was no room in the post-War reparations to the hospital and the machine was placed in Charterhouse Square. The 15 MV linear accelerator had high pulsed output for both photons and

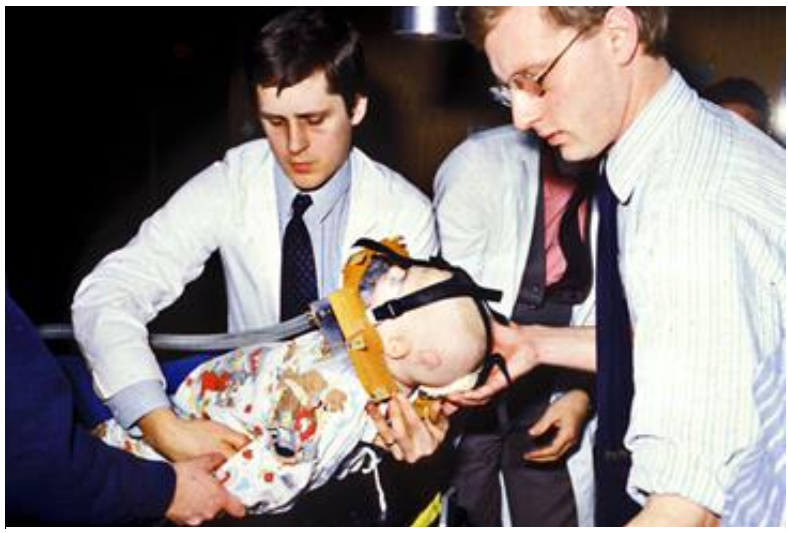
electrons and the Department of Physics – led by the (later) Nobel Laureate: Joseph Rotblat (pictured) and Patricia Lindop from the Department of Radiobiology at Barts, continued radiobiology research on the foregoing aspects of megavoltage radiotherapy for 20 years. The summary of their RBE work was that the RBE of radium and cobalt-60 gamma rays (megavoltage range) and also megavoltage Xrays was approximately 0.86 compared to orthovoltage photons and this changed little thereafter to photon energies up to 25MV. However, as there was no detrimental effect for malignant cells, it did not affect the therapeutic ratio. It explained up to 14% of the difference in the skin reaction, although the majority of the difference was due to the build-up and the absence of the photoelectric absorption from sulphur in keratin.



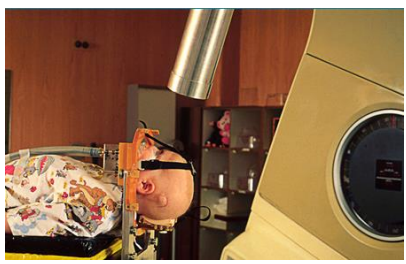
Joseph Rotblat

As time passed and the sophistication of radiation equipment increased, more intricate techniques were born: In Sweden, Leksell had developed the concept of highly focused radiation beams (multiple pencil beams only overlapping at the target distance). His early work was hampered by use of poorly collimated 250kV beams but, later, with the use of up to 200 well collimated 60-Cobalt sources he developed the device that is now called the 'Gamma Knife'. Whereas the previous use of radiotherapy had been based on fractionation (normal tissue, necessarily encompassed by the beams, being spared by exposure to only small, multiple doses of radiation. As reparative powers are lost in cancer cells have (principally the ability to raise their repair 'game' when depleted – a homeostatic reflex that disappears when the cells cross the rubicon to cancer), so fractionation had, from the time of the French radiotherapist: Regaud, become a necessary part of radiotherapy to increase the therapeutic ratio against cancer cells versus normal tissue damage. Gamma knife was different: Here the normal adjacent (innocent bystander) tissues were spared by the fast falling dose gradient at the margin of the target. Consequently, patients treated by Gamma Knife did not need fractionation and were treated by single very large doses of radiation – this was named 'Radiosurgery'. Adaptation of linear accelerators to produce similar isodosimetry to Gamma Knife became a high priority for all forward thinking Radiotherapy Departments and, due the fine efforts of our then Chief Physicist: David Doughty, Barts first introduced linac based radiosurgery into the UK in 1989. Very quickly, within 5 years, over 400 patients with cerebral arteriovenous malformations (the commonest cause of stroke in young people) had been treated with a 1995 publication in the British Journal of Neurosurgery demonstrating equivalent obliteration rates to those by Gamma Knife units (of which there was only one – at Sheffield) at that time.

Over the next twenty years some 20 (numbered) original scientific manuscripts on Radiosurgery have been published from our Department demonstrating the breadth and diversity of this technique. An important manuscript described the acute, subacute (with the phenomenon that later became called: 'pseudoprogression') and late side effects of radiosurgical dose deposition on the nervous – adding to the growing list of radiation effects on the nervous system that have been described from this Department.



Stephen Gill, the neurosurgeon who first developed the Gill-Thomas re-locatable stereotactic frame, and Euan Thomson, a then junior physicist in the Department, who went on to be CEO of Accuray - the firm that developed Cyberknife



Child in Gill-Thomas frame undergoing stereotactic radiosurgery at Barts in 1990 under general anaesthesia

In 1999, the Department acquired a Gamma Knife whose dosimetry proved superior to the linac based system and we moved the practice over to this. Nevertheless, this relocatable stereotactic frame, developed at Barts, was, in its time, an important invention and also had the merit over the Gamma Knife technology of allowing fractionation.

Some of the Barts radiosurgery research manuscripts have probed and questioned the interaction of radiation with biological tissues. For example, the observation that patients treated by radiosurgery for cavernous malformation in brain had a higher rate of complication than AVM was reasoned to be due to the extra deposition of dose in the (iron containing) haemosiderin stained normal surrounding 'cuff' of normal brain tissue, there being an increase in secondary electron flux around the iron atoms. This is another observation from this hospital over subacute radiation reactions on the nervous system.

Later, due to the generosity of the Masons, the Department acquired a Cyberknife (comparable radiosurgical technique to our linac method, but one that uses real time imaging to allow accuracy of localisation and also allows fractionation). Unlike Gamma Knife, Cyberknife technology is not confined to the cranial cavity. This equipment had been developed in California, but even there Barts had influence on its introduction: In the 1980's a very bright junior physicist, Euan Thomson, had been recruited by David Doughty (pictured) to the physics team and had helped in the development of the retinoblastoma, lens-sparing technique and the linac based stereotactic radiosurgery developments at the hospital. Euan moved on quickly in the field and migrated to the USA, where the originator of the Accuray recruited him and he became the first CEO of the company – the company that developed Cyberknife.

David Doughty (in the yellow jacket) at his retirement dinner

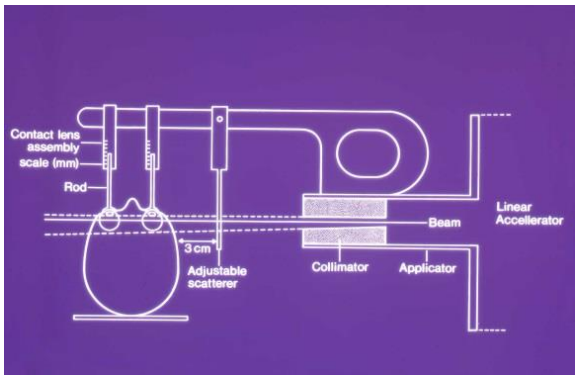
Cyberknife delivers radiosurgery in a different way to Gamma Knife in that it images the target in real time and then, through imaging information channeled through to the robotic arm that holds the small linac, delivers pencil beams of radiation onto the target from multiple node stations. The technique does not require a stereotactic frame pinned to the patient and therefor is not constrained to the cranium. After the introduction of Cyberknife, we have been able to practice radiosurgery to the spine and body and considerably extend the spectrum of diseases that can be successfully treated by radiosurgery. Not only, this but we have been able to compare the Gamma Knife and Cyberknife technologies as we are the only centre in the UK boasting both these radiosurgical techniques.

Cyberknife machine at Barts

The need for highly focal high dose deposition of radiation as single (or a few large fractions) – radiosurgery - (not requiring fractionation to spare collateral damage but depending on the very fast-falling gradient at the margin of the tumour) has proved a very successful extra facility to the Department.

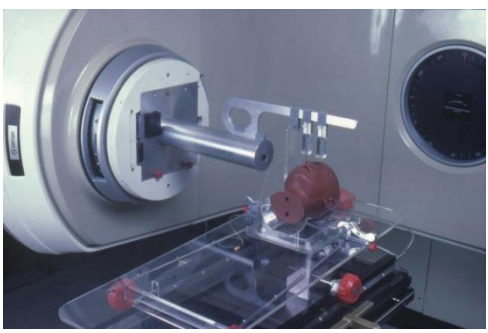
In the early 1980's, in Holland, Jens Schipper devised an ocular radiotherapy method for treating the entire retina (up to the ora serrata) without delivering a cataractogenic dose to the lens. At Barts, then as now, the Ophthalmic Departments Barts/Moorfields refer many patients with ocular tumours and, we developed and adapted this Schipper technique for lens sparing radiotherapy, initially for retinoblastoma cases (that did not have vitreous spread or disease at the ora) but later, many ocular haemangioma. This was perfected and helped several hundred children (usually very young infants and

toddlers) with retinoblastoma to recover without developing cataracts. The technique comprises the development of a non-divergent 6MV Xray beam (due to beam splitting) that was penumbra trimmed (by a secondary collimator) to a high degree, together with a coupling of the eye (by a contact lens assembly connected by a rod-and-ruler to the linac). Once again, David Doughty was instrumental in driving through this new technique. The blue-prints were requested and given (free of charge!) to Stanford, California and Tokyo. With the passage of time and improved chemotherapy, the technique is now used less for retinoblastoma and more to treat ocular haemangiomas, for example, in Sturge Weber disease (reducing their tendency to leak and grow).



Line diagram of the extremely accurate lens sparing ocular radiotherapy technique.

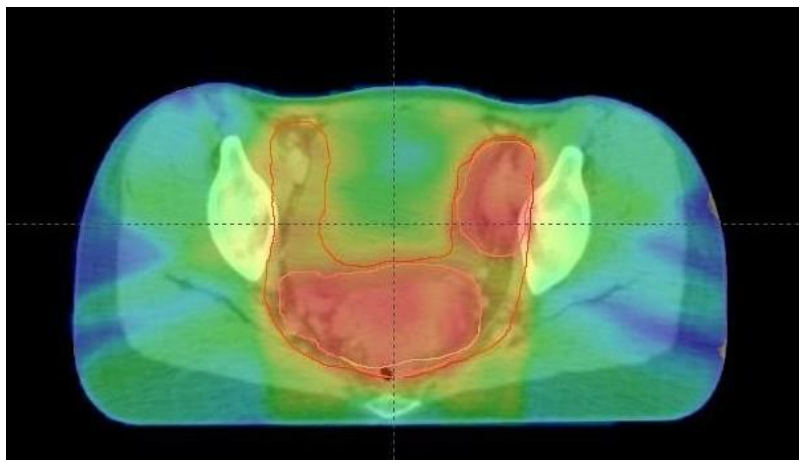
In the diagram above, the beam is "split" down to the central axis (to obviate beam divergence) and a secondary collimator (almost out to the treatment distance) reduces penumbra to tiny proportions. Then, the eye is both fixed and coupled to the treatment machine by a contact lens and rod assembly.



A Phantom assembly with an extractable phantom eye – used to dosimetrically verify the assembly before introduction into clinical practice

With the turn of the 21st Century and the development of Intensity Modulated RadioTherapy (IMRT), a new era for the subject world-wide was born in that it

was now possible to mould the dose more 'conformally' than ever before to the targeted tumour. The ability to alter the fluence across the radiation portals allowed the clinician to produce low dose concavities in a high dose radiation volume. Barts has been performing this technique in routine service for a decade now. Dr Melanie Powell's Barts' team with Rodney Reznek and Alexandra Taylor were the first to demonstrate the fact that the pelvic nodes ran within 0.75 cm of the (identifiable on scan) pelvic vasculature. With the ability to map these nodes came the ability to treat the first echelon of draining nodes (principally from cancer of the cervix uteri) without treating large swathes of the pelvis. The coupling of the knowledge of the anatomic location (relative to large blood vessels) of the regional nodes requiring radiotherapy and the ability to refine radiation coverage to irregular volumes (by virtue of IMRT) allowed this important advance in our subject. This work from Barts gave a great boost to modern Gynaecological Radiotherapy, enhancing the sophistication of pelvic radiotherapy (which had a chequered past due to late bowel toxicity). This node mapping, relative to anatomic structures that were visible on scans and coupled with the IMRT technology was adopted later for other sites e.g. the head and neck radiotherapy.



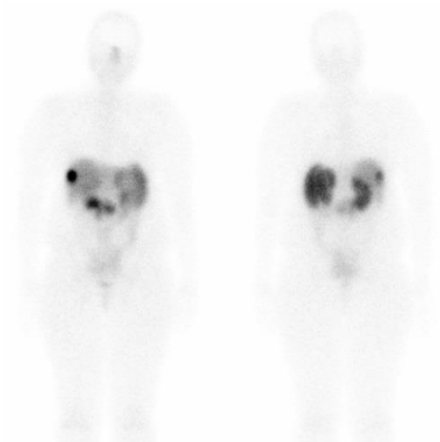
Axial CT pelvis demonstrating the isodosimetry of Intensity modulated pelvic radiotherapy (IMRT) for cervix cancer, utilising the node mapping technique developed by the Barts' team. The ability to mould the high dose around highly irregular target volumes has only been possible since the advent of IMRT and when combined with the node mapping (relative to blood vessels) the safe curative radiotherapeutic treatment of cervix cancer has advanced significantly has progressed greatly. Note that the involved left pelvic side wall nodes are receiving high dose, whilst the central pelvic bowel is spared.

Gynaecological radiotherapy remains a subject where brachytherapy is

important – the practice of brachytherapy in, say head and neck cancer, has dwindled over the years, largely due to the increasing sophistication of external beam techniques. However, Dr Powell's team have the most advanced brachytherapy machines and Barts remains a national centre of excellence for Gynaecological radiotherapy.

Prostate brachytherapy is also practised in the Hospital for early cases and Dr Paula Wells heads a service that offers this to selected patients, for whom it represents a low morbidity method of cure.

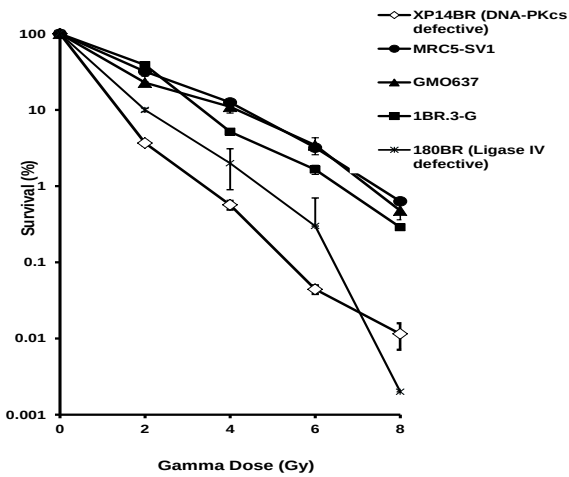
With regard to unsealed source radioisotope therapy, 131-iodine has been in use at the Hospital since the Second World War to treat thyroid conditions (thyrotoxicosis and cancer). The extension to other isotopes for imaging and therapy has been an interesting progression. For example, recently, the use of octreotide (a somatostatin analogue targeting a specific receptor on neuroendocrine tumour cells) as a conveyor of the radioisotope 177-Lutetium to the tumour cells (where the isotope delivers cytotoxic radiation) has recently become a routine part of therapy options in this disease.



Post-therapy scan after 177-Lu octreotate therapy for neuroendocrine cancer metastatic to liver. New radioisotopes such as this are changing and expanding the role of radioisotope therapy in cancer

It is established that there are polymorphisms in the population that are unusually sensitive to radiation. Usually such patient have defect in DNA repair. Such defects also select for carcinogenesis and so it is more likely that they will come to radiotherapy. Patients with ataxia telangiectasia are extremely sensitive to radiation and we have had cases of this who have been damaged by standard dosages of radiation. One unfortunate case referred to the Department had the syndrome but without either ataxia or telangiectasia a *forme fruste* of the syndrome who suffered severe toxicity from routine doses of radiotherapy.

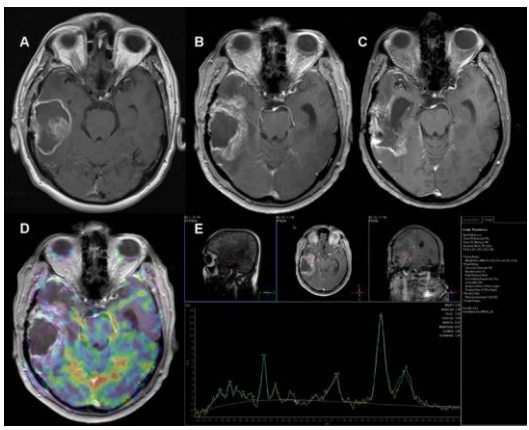
Other syndromes exist of exquisite sensitivity and the Barts' Radiotherapy Department has described two new syndromes viz. DNA ligase 1V deficiency and an extraordinary case of Xeroderma pigmentosa (which is usually a hypersensitive condition to ultraviolet and not ionising radiation) who proved excessively sensitive to radiation (a Protein Kinase PKcs deficiency that was separate from the xeroderma pigmentosa genetic fault – proven in vitro when our team (Brunel University/Barts) spliced back the normal gene into the genome of the cells correcting the ionising radiation fault but not the UV sensitivity).



Cell survival plot following radiation exposure to different doses. Three normal cell lines are compared to two newly recognised radiation sensitivity syndromes discovered at Barts viz. DNA ligase 1V deficit and Xeroderma Pigmentosa DNA PKcs deficiency.

Following on from published observations on five excessively radiosensitive patients, our joint laboratory project with Brunel University again received funding from another Sassoon – this time Vidal (another branch of the family and of hair dressing fame) - and the Brunel University laboratory group, under the leadership of Chris Parris, have developed a fast laboratory test of clinical radiosensitivity that can be run prior to radiotherapy (based on H2AX histone expression over time after radiation) on a patient's white blood cells. Where a patient has an unusual cancer at an early age, has a strong family history of cancer, a cancer predisposition syndrome or has an unusually severe myelosuppression with antecedent standard dose chemotherapy, then this test is worthwhile prior to the start of radiotherapy. This co-operation with Brunel has proved fruitful and currently we have a MD research fellow performing a project in the lab – studying the response and repair from radiation exposure of unusual cell lines derived from patients that have passed through our clinic (Li Fraumeni, BRCA with PMS2, BRCA with separate mRNA splicing defect, Temozolomide hypersensitivity and a series of ocular melanoma cells that all have BAP-1 defects).

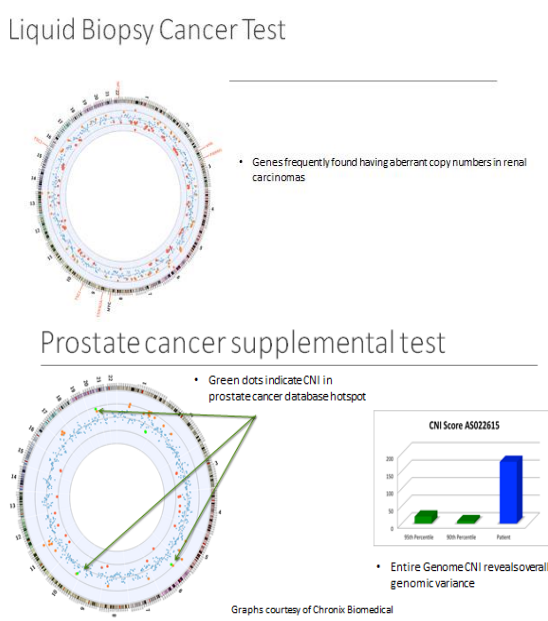
With regard to observations on unexpected clinical sequelae from radiotherapy, it has been already mentioned that Professor Arthur Jones' great strength was in clinical observation and, following his training in neurology prior to entering our subject, many of his observations were of a clinical nature. His observation that following cervical (spine) radiotherapy, patients often developed Lhermitte's sign a few weeks later was such an observation and he subsequently, by serial observation, noted that it had no late sequelae and reasoned that it was due to transient demyelination of the cord which was later repaired. He also made other analyses quae radiation sensitivity of the normal nervous system. Later, during our radiosurgery work, we were the first to formally describe the subacute swelling phenomenon that occurs after radiosurgery to some slow growing tumours –such a meningioma and neuroma. Interestingly, this has later been showed to have parallels to what is referred to 'pseudoprogression' (see image below), a phenomenon that is observed in gliomas responding to therapy. This term refers to an MRI appearance previously attributed to tumour progression but actually represents an inflammatory response to therapy, comparable subacute necrosis/inflammation following radiosurgery for benign brain tumours). The neuro-radiology Department at the hospital and in particular Dr Anant Krishnan and Dr Jane Evanson are now concentrating their imaging expertise on attempting to more accurately distinguish this phenomenon from real tumour growth after therapy – PET, MR spectral content and MR perfusion studies.



Pseudoprogression in a 64 year old man with a right temporal glioblastoma: A. T1 post contrast MR image reveals a peripherally enhancing mass lesion in the right temporal lobe prior to the commencement of adjuvant chemoradiotherapy. B. T1 post contrast MR imaging after completion of radical radiotherapy and adjuvant chemotherapy, demonstrating an increase in the enhancing component of the lesion in the right temporal lobe. C. T1 post contrast MR imaging 6 months subsequently shows a decrease in the enhancing component. D. Fused T1 post contrast and cerebral blood volume images reveal the area of enhancement does not have an associated increase in cerebral blood volume as would be expected in tumour progression. E. Single voxel spectroscopy demonstrates large lipid and lactate peaks in keeping with a treatment-related effect. The choline

peak is elevated with consequent reductions in creatine and N-acetylaspartate in keeping with the presence of pre-existing tumour in this region.

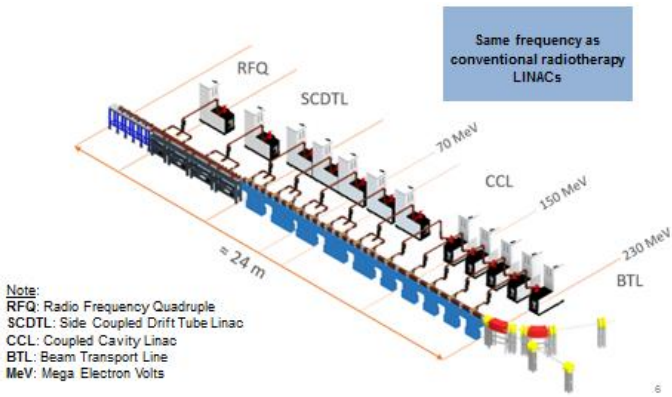
Members of the department are involved in research which is at the forefront of Oncology for tomorrow. Next generation sequencing has allowed the exploration of DNA in the plasma (for tumour DNA is circulating in enough quantity for this test to be used for screening, detection of minimal residual disease and, excitingly, to monitor the mutations of driver genes during the natural – or perturbed – history of a cancer over time). This has enormous implications for Oncology. Use of cell-free DNA techniques for next generation sequencing (NGS) analysis in advanced cancer, based on plasma circulating DNA fragments from a patient with advanced renal cancer and, in another individual prostate screening on Barts' patients – both in 2015 (Barts/Gottingen/Chronix Biomedical joint project).



Top panel demonstrates a 'circos' plot of a cancer's genome (reconstructed from circulating, cell-free DNA, using 10 ml of the patient's plasma) demonstrating many mutations (orange dots) and a high genetic change index. The lower plot demonstrates (in a prostate screening case) the abnormal genetic change index and mutations corresponding to known prostate "hot Spots" – the green dots that correspond with the orange mutations observed – in a patient who is highly likely to have early prostate cancer.

In the field of radiotherapy, there is currently much interest in the use of charged particle beams as these will deposit a radiation dose equivalent (in terms of ionising events/bond breakages in DNA) to xrays/photons but, due to the Bragg peak phenomenon, deposit their energy at a depth (that is controllable by energy changes) and have little entry dose and no exit dose. This has enormous advantages for paediatric radiotherapy in particular but also for adults practice. To this point in time, the only 38 facilities offering proton beam

radiotherapy in the world are utilising cyclotron technology – extremely expensive, hugely space and resource occupying and relatively slow in the ability to modulate dose deposition. Over the last few years, the Particle Physicists at Cern (Hadron Collidor) have invented a 'linac based' proton facility and a small British firm has acquired the rights to this invention. A member from the Barts department is involved and has the agreement of the City of London architect to, in principle, place a linac proton machine under the East end of the Smithfield car park – a cavernous space close to Barts and under the meat market. It will be of great interest to see if this comes to fruition as it may change the subject of Radiotherapy for ever – another exciting possibility for Barts.



The Linac based proton machine which may come to Barts soon

With the move to the new hospital and the acquisition of chest and cardiac services, the opportunity for new research into chest tumours affords new and exciting possible other joint ventures in the near future.

In conclusion, the Radiotherapy Department at Barts represents one of the most famous specialist Departments in the field of Radiotherapeutics and Clinical Oncology and continues to be at the forefront of the subject.

Epilogue

Nicholas Lemoine
Professor of Molecular Oncology
Director of the Barts Cancer Institute

It is evident from this monograph that there is one word that is used repeatedly by all contributors and that is "privilege" – that is how working here at Barts feels. The preceding memoires reflect not only this sentiment, but also highlight just how much is owed to Barts and the people who worked here in the advancement of our understanding of cancer and its treatment. As the current Director of the Barts Cancer Institute, and a previous Clinical Director for Cancer Services, the heritage that we must live up to is never far from my thoughts and remains a driving force as we strive for excellence in all our endeavours in tackling cancer.

Barts – Charterhouse Square September 1977

My own memories of Barts start in 1977, when I enrolled as a medical student here. It was a beautiful afternoon in Charterhouse Square, the sun shining, the grass still green after one of the hottest summers on record - a truly lovely day. If you come here today, it will probably strike you as just the same. I remember a group of young people gathering tentatively in the corner of the Green outside College Hall (now Dawson Hall) and starting their first steps on the journey that is University, and perhaps most particularly Medical School as a formative experience. I even met my wife that afternoon, showing that Barts is truly a fount of creativity for both personal and scientific development!

Who else was there? Tim Spector, now Professor of Genetics at Kings College who has made a fantastic career out of the genetic analysis of twins. His father, Wally Spector, was perhaps the most inspirational figure of his era in basic pathology and I was privileged to be able to learn from him at Barts, not just the facts of the matter but the opportunity to challenge the dogma and initiate research into new ways of thinking about disease and its management. Amit Oza, now Professor of Medicine at Princess Margaret Hospital and University of Toronto. Brian Stevenson, now Consultant Surgeon at Newport Gwent Hospital and Dave Ralph now Consultant in Andrology at University College London were my usual partners in crime. Bikes, birds and booze seemed to frame our lives in those early days and we soon learned that only by making sure the correct pair from the three was used, it worked out alright and anything

else did not. Midnight racing on motorcycles around the square, before today's killjoy speed-humps, was a regular feature enjoyed by our group, if not by the rest of the residents of College Hall who from all six floors would pelt us with milk cartons and worse! It didn't matter as long as I won, but with me on a Yamaha RD250 (my pride and joy, a race bike replica) and David Crossman (now Dean of Medicine at St Andrew's University) on a Honda CB500, which I thought was the height of cool at the time but now I know is a grandad's bolide of choice, it did not always play out well...

To the bar – we were young, after all. Yes, I know that Barts Cancer Institute has since established special standards for entertainment, but it was not always so here in the Square. Beer was the liquid that made the world go around, although a lot of it appeared to be on the floor, not least as a consequence of the most toxic drinking challenges known to man or woman. Where we now have our secure Tissue Bank freezer complex in Dawson Hall was once the bar for the medical school. It did not open any evening until 10pm and I cannot remember when it closed (*hhmm*...), but a fixed presence in the early hours of the morning on a stool at the bar would be a Police Constable from Snow Hill Police Station around the corner from Smithfield Market, just 'doing his rounds' of the district, with a complimentary pull of the beer tap whenever he needed. An hour's sojourn and he was always reassured about the safety of this particular corner of the City of London. Also conspicuous was Percy, a huge wooden mascot for our rugby club, weighing in at probably half a ton, immutable and immovable – until he was kidnapped one night by St Mary's Hospital rugby team with a crew of burly young men and a flatbed truck. Needless to say, he was recovered subsequently and suitable retribution exacted in Paddington. Happy days, bloody noses.

To the wards - as we must if we are to learn. Teaching rounds at 7am, a challenge for students at the best of times and I wonder what the students of today would make of this now. Only one firm of consultants made this mandatory and needless to say this was Andrew Lister, Ama Rohatiner and the team. It was a challenge worth meeting as I don't think that I have ever learnt at such a pace and with such intensity. Medicine was brought alive through being with patients who were facing death, and these brave and deeply compassionate young physicians who were doing all they could to rescue them. I was not the only one who felt inspired through seeing every patient as a human in need, but also an opportunity to learn to do better.

The paediatric oncology wards in Kenton and Lucas Wing were both harrowing and inspiring. You will have read of Jim Malpas, Judith Kingston and John

Lilleyman earlier, but it was a result of seeing their work that my elective period for two months as a medical student was spent at the Paediatric Oncology Unit at Great Ormond Street Hospital. How times have changed, and so much for the better, as they have explained.

At this point as a medical student, I also encountered Nick Plowman for the first time. His brain functioned orders of magnitude faster than mine could then, but experience of being in the radiotherapy clinic beside him made me recognise that you only get out what you put in. I spent hours in the library researching radiation physics so that I could aspire to have the same level of insight into the technology to allow me to understand what he was offering his patients for the best outcome possible. I also sat watching what I know to have been a (very) young consultant, counselling the patients in the most wonderfully human way about what they faced. A concept that we now define as empathy, but then we just recognised as a quality in a doctor whom you would wish your own loved ones to be cared for by. I am coming back to you all later, with the perspective of thirty years' experience.

Barts – Charterhouse Square May 2005

It is a beautiful day again. I had spent the last eighteen months getting our labs built and commissioned here, while still running our research unit at the Hammersmith Hospital in West London. One of the most wonderful things on this day is to bring our Unit's staff – every single one of them, including Pam Charles, my assistant for over twenty years – from what felt like working in the salt mines next to Wormwood Scrubs Prison (literally – I realised it was time to leave when the warders at the entrance knew my name...) to the sunlit uplands of Charterhouse Square.

I owe a debt of gratitude to Professor Sir Nicholas Wright, the then Warden of the Medical School, for his vision in establishing a cancer institute at Barts, and for making me Director! He gave me a free hand in building the BCI and we exploited it to the full, to create an environment that is open and supportive to all. No longer individual labs closeted away, but cohesive research Centres, with large, sweeping open-plan environments, and core facilities underpinned by talented staff who give their all – you know who you are, and I hope that you know how much you are valued. The fantastic contribution from Delphine Purves, who is the epitome of 'the power behind the throne', the wonderful support of Ian Hart and then Kebs Hodivala-Dilke as Deputy Institute Directors, and of Kaye Yeung, who almost single handedly has dragged us from being a precious "research-only" centre into highly regarded teaching institute, and the imagination and energy of all the scientists, clinicians and staff who

work here has been simply incredible over the years. You can read more about my remarkable colleagues and of our achievements in Ian Hart's contribution.

In developing the strategy of the BCI, I quickly realised that in order for our translational aspirations for cancer research to be of clinical benefit, we had to work closely with the clinical cancer services at Barts hospital and work hard to ensure that our clinical services are top-notch. Therefore, over the last decade, I dedicated myself as Clinical Director for Cancer Services at Barts & The London NHS Trust and then as Director of Research & Development for Cancer & Surgery at Barts Health NHS Trust. When he was Deputy Director, and often called upon to be my drinking partner, Ian Hart described it as 'a dirty job, but someone's got to do", a phrase that could equally be applied to the two jobs that I had to do in the NHS!

Alongside our development of the BCI, from 2007, we also initiated and managed the Central and East London Comprehensive Local Research Network (CLRN, now the North Thames Clinical Research Network), one of 25 in the UK. Part of the National Institute for Health Research (NIHR), the CLRN was a means of encouraging and supporting NHS Trusts in the region to be involved in clinical trials, to maximise opportunities for patients to be involved, and for which the CLRN provided income to cover the costs to the NHS. In persuading Delphine Purves to take on the senior manager role (in addition to her BCI role), famously describing it as "money for old rope", I was perhaps a tad economical with the truth, as the work (and bureaucracy) increased exponentially! The reason for this ever-increasing workload was that our CLRN became arguably the biggest and best in the UK (with the most clinical trials opened and the most patients recruited). Unsurprisingly, we gave up our dual roles in 2013, after six years of pain, but we built something of which we were rightly proud. Now, as the Medical Director of the NIHR's new CRN, I remain committed to the NIHR's goal of ensuring that the UK and the NHS remains an international powerhouse for clinical research.

Barts – Charterhouse Square June 2015

In Ian Hart's contribution, you have read a lot of the recent history through the RAE and REF exercises that have cemented the Barts Cancer Institute as one of the UK's key contributors to international excellence - the 2012 McKinsey Review accorded a World's Top Ten ranking for the BCI against University cancer research departments. I am proud to be part of Barts Cancer Institute's past, present and – I hope – its future. But what does the future hold?

I can envisage our strategy following our current research pathway, which

relies on the interdisciplinary and integrated ethos of the BCI, where research flows naturally from bench to bedside, fed by a strong co-operative culture and service support. We must strive to maintain our strong sense of community, with the emphasis on group-driven research, creating a highly collegiate, collaborative and sociable environment.

I believe that more and more, particularly through our cancer clinical trials, we will improve our understanding of precision (personalised) medicine, overcome drug resistance, explore combination therapy and develop better biomarkers for rapid and accurate diagnosis.

We must, of course, continue Barts' long tradition of helping to train the cancer research workforce of the future, taking the brightest young scientists and doctors through our PhD programme that gives them exposure to cutting edge developments in the laboratory and in clinic trials, equipping them with the skills ultimately to develop their own programmes.

As we continue to focus on our unique areas of research expertise and achieve our research objectives, ultimately, we become part of the legacy at Barts, recognized as one of the major contributors to decreasing the mortality and morbidity from cancer and enhancing the quality of life for those with long-term malignancies. And, to end as we began, with the words of Percival Pott, we will make "Every rational attempt toward relieving mankind from such an evil".

Acknowledgements

I pay particular thanks to Chris Gallagher, who was the previous Clinical Director, as well as Andrew Lister, Jamie Cavenagh, Nick Plowman, Amen Sibtain and my current colleagues Sarah Slater (Solid Tumour Oncology) Virginia Wolstenholme (Clinical Oncology) and Heather Oakervee (Haemato-Oncology). Lisa Hollins and Frances O'Callaghan are senior NHS managers who really care about our research capability as well as our capacity to care for our patients, and I salute them both. Claire Murrell as our Head of Cancer Nursing has always been absolutely inspirational, and I am so pleased that she has chosen to come back and join us in a new career as Cancer Research UK's Lead Cancer Nurse. Finally, I must pay tribute to my Personal Assistants; things got off to a rocky start with a revolving door of ten PAs coming and then going over a period of 14 months citing the stress of the role as unbearable! When I am holding down four jobs simultaneously, they are too of course…. However, Blanca Kase and more recently Irene Bouwer have proved equal to the challenge

as well as brilliant fun to work with.

For the CLRN, I thank all our team, particularly Dr Marta Buszewicz, the Deputy Director, Alastair Nicholson, our lead Research Management and Governance Manager (now leading the roll out of the new trials permissions process at the Health Research Agency), John Sheedy, our Finance Manager, and Marjia Monsur, our Coordinator, as well as our Executive Board, who not only contributed to the strategic operation of the CLRN, but lightened our load by making it all such fun!

Finally, we owe a depth of thanks to all our donors and supporters, without whose great generosity none of the work we do at the Barts Cancer Institute would be possible.

"I can honestly say that the best 8 years of my academic career were those I spent at Barts: the last of my working life...I look back on this era as the pinnacle of my career." Professor Emeritus Ian Hart

"The clinical and academic contribution any radiologist can make is greatly dependent on a close working relationship with interested, enthusiastic colleagues. It was my great good fortune while at Barts to have worked with outstanding colleagues and friends." Professor Emeritus Rodney Reznek

"The most special thing about the department [of Haemato-Oncology at Barts] was the sense of working with like-minded people, whose aim was always to be thinking in terms of developing curative treatment." Professor Emeritus Ama Rohatiner

"I regard my time at in the Chair at Queen Mary and as a consultant at Barts and the Royal London Hospital as an honour and a privelege."
Professor Emeritus Sir John Lilleyman

10 YEARS' CELEBRATIONS

Barts Cancer Institute
Queen Mary University of London