JAMES IV ASSOCIATION

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James IV Travelling Fellowship Report

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Overview

The James IV Association Travelling Fellowship provides an exceptional opportunity to visit and interact with people and institutions around the world and to learn and reflect on the clinical, research and organizational aspects of surgical life.

This Fellowship allowed me to visit selected leading centres in the US and Australia in my areas of clinical interest (breast cancer, oesophageal cancer), scientific interest (translational research) and clinical audit. I gained a personal education as to how health care systems work differently in terms of their function and working practices, but at the same time the marked similarities of the clinical and scientific problems we face together were a source of academic reflection.

While one is bound to be selective in distilling multiple interactions over several weeks into a brief but coherent summary, the Professor Murray Brennan question "what one thing did you learn today?" remains a good way to focus on the many learning points; some of the highlights are presented here.

Host Institutions

The institutions visited were selected (with some difficulty) to embody centres of excellence in the fields of translational medicine (the laboratory/clinical interface) and clinical audit from the wide range of places. In some settings there were individuals with whom I had already corresponded (including Gabriel Hortobagyi and Laura Esserman) or who had already visited Dundee (Bruce Barraclough, Mary Helen Barcellos Hoff); all were extremely welcoming and willing to share ideas and spend time looking after a foreign visitor. The Fellowship was split into two blocks of time (October/November 2005 and February 2006) which had the advantage of allowing pause for reflection between visits and thus enhanced the development and exchange of ideas.

The host institutions were:

MDAnderson, Houston, Texas, USA
24th October - 4th November 2005
Principal hosts Professor Gabriel Hortobagyi, Professor Kelly Hunt, Professor Steve Swisher; including additional discussions with:

Wayne Hofstetter
Rosa Huang
David Gershenson
Francisco Esteva
Massimo Christofanilli
Stacy Moulder
Lajos Pusztai
Raphael Pollock
Dihua Yu

Memorial Sloan Kettering Cancer Centre, New York, New York, USA
5th November -12th November 2005
Principal hosts Professor Murray Brennan, Dr Pat Borgen
Bridget Fahy
Patrick Borgen
Teri Cohen
Tari King
Marty Wiser
Chip Cody
Larry Norton
Yuman Fong
Carlos Cordon-Cardo

University of Califonia, San Francisco, USA
3rd February – 10th February 2006
Principal host Professor Laura Esserman
Rob Foster
Cheryl Ewing
Cathy Park

Lawrence Berekley Laboratory, San Francisco, USA
7th February 2006
Host Professor Mary Helen Barcellos Hoff

Roche Diagnostics, Pleasanton, California, USA
9th February 2006
Host Dr Lin Wu
Nancy Patten
Sim Truong

Sydney, New South Wales
11th February – 17th February 2006
Principal hosts Professor and Mrs Bruce Barraclough
National Breast Cancer Centre
Helen Zorbas
C CORE (Liverpool)
Michael Barton
Geoff Delaney
Val Poxon
Breast Cancer Institute of NSW (Westmead)
John Boyages
Owen Ung
James French
Sax Institute
Sally Redman

Cancer Institute of NSW
Jim Bishop
Garvan Institute:
Catriona McNeil
Euan Miller
Warren Hargreaves
Dave Segeva
Clinical Excellence Commission
Bruce Barraclough
Cliff Hughes
Bernie
Sarah
Bowral Hospitals, NSW
Andrew Leicester

Seminars given

Since one benefit of the Fellowship is to exchange ideas, it was a privilege to have the opportunity to present 30-60 minute seminars on translational laboratory data and clinical audit data to a range of audiences in the USA and Australia. These seminars included:

- P53 and Breast Cancer
- P53 in breast and oesophageal cancer
- Surgical Hospital Volume Does Not Influence Long Term Survival for Oesophageal or Gastric Cancer
- Audit Informing Practice and Policy
- What More Can We Learn From Population Based Cancer Audit
- Processes, Procedures and Barriers to Successful Audit

Selected title slides are presented on the back cover of this report.

Clinical Practices

As an immediate prelude to the Fellowship visits, I attended the 58th annual MD Anderson symposium on cancer research entitled 'Discovery, Validation and Integration of Molecular Markers and Molecular Imaging: Toward an Implementation into Clinical Practice'. This brought together international expertise including those who have established gene array technology as clinical diagnostic tests, experts in biomarker discovery and validation and cutting edge imaging (molecular, PET, MR) for both human and small animal use.

Given my interest in the application of microarray to clinical material (including as the UK Principal Investigator for the MINDACT study) and as Deputy Director of the Clinical Research Centre in Dundee (which will house these imaging technologies and promote their use in animal models and early phase clinical trials), this meeting was a refreshing update on the current state of technologies from an international perspective. It also highlighted the areas for focus and improvement at my home institution.

At the MD Anderson, Memorial Sloan Kettering, UCSF and Breast Cancer Institute of New South Wales, I experienced clinics, operating sessions, multidisciplinary meetings and one to one discussion.

Clinically, it was helpful to discuss the technical management of the axilla and the use of scintigraphy to pinpoint the relevant nodes in sentinel node biopsy (MD Anderson) and sentinel node biopsy for neoadjuvant treated patients (MD Anderson and MSKCC). The latter is an area where we should follow in UK surgical practice, particularly as we gain increasing experience with neoadjuvant patients. Whether this applies equally to neoadjuvant endocrine therapy (widely used in the UK but not the US) compared with chemotherapy is uncertain. There are striking differences in the funded use of chemotherapy agents between the US, UK, Australia but a low use of endocrine therapies in US patients. With moves to neoadjuvant therapy for DCIS and low dose oestrogens for menopausal symptom relief this presents opportunities for collaborative clinical trials, for example the ACOSOG neoadjuvant comparative trial of three aromatase inhibitors.

The use of ultrasound directed fine needle aspiration cytology of axillary nodes, MRI and PET scanning to determine axillary therapy is less likely to become widely used in the UK resource-constrained practice. However, ultrasound directed fine needle aspiration cytology may well become more widespread in the UK.

In contrast, in the interactions between surgical oncology and reconstructive surgery we appear to be more adventurous in Dundee than some centers worldwide: the controversies ranging over which techniques to use in breast reconstruction and in particular the irradiation of TRAM and DIEP abdominal autologous tissue flaps is one area where we can usefully contribute to the international picture. Our Dundee practice has a relatively large experience of flap irradiation which we would like to compare with those in UCSF (in favour of immediate reconstruction and flap irradiation) and the MDAnderson (where practice has moved to more conservative, delayed reconstruction. On the other hand, using more allograft material, prostheses and internal rotation of breast tissues to fill defects following breast conservation is one area for development. Following, and largely driven by, the experiences on the Fellowship, I will be combining the East of Scotland Breast Service with the regional Plastic and Reconstructive service in an integrated ward, treatment areas and clinical offices complex; this mirrors the particularly close integration witnessed in MSKCC and UCSF.

In my other area of clinical interest, the impressive results from the MDAnderson in oesophageal cancer through the use of neoadjuvant therapy and chemoradiotherapy and high quality perioperative care has increased the 5 year survival for oesophageal cancer

to 40% compared with world averages of 27%. This suggests that enhanced survival may be achieved in oesophageal cancer, as in breast cancer, by applying the therapeutic knowledge we already have to appropriately selected patients. Perhaps focusing on multidisciplinary management rather than hospital volume effects may do for oesophageal cancer what was achieved a decade ago for breast cancer.

Research

Many colleagues I met also engage in active translational or audit research; others have forsaken clinical practice altogether to focus on laboratory analyses of clinical problems and clinical materials. The importance of setting aside quality time for research separate to clinical activity appears to be a vital component to contributing high quality research using clinical material. There were clear advantages in some settings of having the research laboratory distinct from the clinical area (eg Garvan institute in Sydney), or attached by lengthy corridors (MD Anderson) or in adjacent buildings (MSKCC) allowing some separation of duties and focus on either clinical practice or research, one at a time. However, too great a distance appeared to cause a detachment between clinical input and laboratory research, with email and foreign visitors being the catalyst for local activity!

For me three key areas of change in approach to translational research have come out of the Fellowship.

Firstly, developing an overall schema for breast cancer research - applying the translational model that has been so successful for bladder cancer used in MSKCC (Professor Carlos Cordone-Carlo) to multidisciplinary breast cancer research is now underway in Dundee.

Secondly, more focused international collaborative research: with the Lawrence Berkeley Laboratory - the relevance of normal stem cells and breast cancer stem cells to the TARGIT intraoperative radiotherapy translational research programme; interactions with Roche Diagnostics to test their p53 mutation detection chip against breast and oesophageal cancers; developing breast cancer p53 research with colleagues in MD Anderson.

Thirdly, as Deputy Director of the Clinical Research Centre in Dundee which will house MRI and PET imaging technologies and promote their use in human studies and clinical trials, the visits have pointed how to successfully drive this facility forwards.

Organisational Issues

In the institutions I visited, the clinical practices and research clearly depend on well organized service delivery and laboratory programmes; clinical audit similarly requires an integrated approach to linking data sets and using data to facilitate change.

On a number of levels, short, focused meetings - for example the weekly meeting with clinical research fellows at MSKCC, the seminar style research lectures with a range of talks, senior input and appropriate timing (for example early morning) so that most people can make the meeting - clearly give a buzz that drives enthusiasm at all levels. This dynamic educational environment could well develop into a planned 2 week postgraduate exchange between MSKCC and Scotland.

Different clinical setups highlighted the integral use of input from non medical practitioners in a US setting. The large centres emphasized the need for multiple clinical multidisciplinary meetings; smaller centers successfully demonstrated an alternative approach of running the multidisciplinary meeting in the middle of the clinic so that multiple consultations between the patient and different clinical disciplines can occur. In New South Wales the use of videoconferencing worked well where geographical separation would otherwise prove prohibitive for multidisciplinary interaction. There is also a clear advantage, at least in a US setting, of dividing research into discrete areas with individuals responsible for delivering in each area.

There are notable similarities between New South Wales and Scotland in terms of geography, population, information provision and gaps in care with data linkage for increasing the effectiveness of data already gathered - a challenge we both face. A development of audit between Scotland and NSW is currently under consideration: developing a common taxonomy for future mortality audit will allow comparisons between different health care systems; this has been greatly facilitated by the travels to Australia.

Final reflections

I listened with interest to the debate during the James IV Association meeting at the Royal College of Surgeons of Edinburgh 500th Anniversary Celebration as to the age at which the Fellowship should be awarded. As one who was age 43 years at the time of award, who travelled age 44 and then 45 years, I would contend that the 43 ± 2 years has worked well for me. As an established clinician researcher with increasing demands on one's time, a brief timeout to travel to meet people, visit places, compare practices, discuss the problems shared the world over, and pause for reflection is exceptionally valuable.

I have special thanks for the professional and organizational skills of Gabriel Hortobagyi and Ann Pearce (MD Anderson), Murray Brennan and Terri Cohen (Memorial Sloan Kettering), Laura Esserman and Mary Lyall (UCSF) and Bruce and Beverley Barraclough (Sydney, New South Wales). They made the travel easy, the arrivals welcoming, cured jet lag with fresh air and sunshine and were wonderful hosts. I also had the good fortune to meet some exceptional patients who I thank for their forbearance. Back in Dundee, I am particularly grateful to Isobel Anderson (Personal Assistant) and my clinical and laboratory colleagues for holding the fort during my travels.

Finally, I wish to thank the James IV Association for giving me this exceptional opportunity, as originally envisaged by Ian Aird, John Bruce and William Hinton, and believe the Travelling Fellowship will be pivotal for me, as it has been for so many others, in directing my future surgical vocation.

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