LETTER TO EDITOR



Contribution of Surgeons from Cardiff in Improvement of Research and Care in Breast Disease

Anurag Srivastava^{1,2}

Received: 28 April 2021 / Accepted: 10 May 2021 \odot Association of Surgeons of India 2021

Cardiff Breast Unit a part of Department of Surgery, University Hospital, Cardiff University Wales UK, has a remarkable record with some notable names in the history of breast surgery and medicine. A description of some of the stalwarts from this single unit is narrated by the author who has witnessed and interacted with some of the breast surgeons from Cardiff. Some pertinent references at the end give a bird's eye view of the "Body of Work" published by the Cardiff breast surgeons described in this article.



Anurag Srivastava dr.anuragsrivastava@gmail.com

² Department of Surgical Disciplines, All India Institute of Medical Sciences, Ansari Nagar, New Delhi 110029, India

Sir Andrew Patrick McEwen (APM) Forrest FRCS FRCPEd FRSE was born in 1923, studied medicine in the University of St. Andrews, and returned to Dundee following Military Service and surgical training in the Royal Navy. He served as a research fellow at the Mayo Clinic for a year and later joined Glasgow as lecturer and then senior lecturer to Sir Charles Illingworth. He became the fellow of all the three British Royal Colleges of Surgeons and was awarded the degrees of MD and ChM with honours and gold medals. Soon he adorned the Chair of Surgery at the Welsh National School of Medicine in 1962, which he occupied till 1971when he was appointed the Regius Chair of Clinical Surgery at the University of Edinburgh. His research interest in breast cancer led to the development of a comprehensive clinical service at Cardiff for women with breast cancer. He was Chairman of many national committees of breast cancer including the working group which recommended the introduction of breast screening as a part of the NHS, the Breast Cancer Research Subcommittee, and the Scottish Advisory Committee on Breast Screening. Professor Sir Patrick Forrest retired from the Regius Chair of Clinical Surgery in the University of Edinburgh in 1988. He subsequently became the Chief Scientific Adviser to the Scottish office.

Sir Patrick was the President of the Surgical Research Society and the Association of Surgeons of Great Britain and Ireland and a member of the Medical Subcommittee of University Grants Committee, Medical Research Council, Advisory Board for Research Councils, the Scientific Advisory Committee of the Cancer Research Campaign and the Council of the Royal College of Surgeons of Edinburgh. His achievements in the field of breast cancer earned him the Lister Medal by the Royal College of Surgeons of England in 1987. He chaired the Department of Health working group on the implementation of National Health Service Programme on nationwide breast cancer screening. His thinking on breast Screening was greatly influenced by Maureen Roberts who he had recruited to join his team in Cardiff.

BALCO Medical Centre Raipur, Naya Raipur, Chhattisgarh 493661, India

He was ahead of his times, proposing a minimal access approach to axilla and perhaps the first surgeon to conceive the idea of "pectoral node biopsy later named axillary four node sampling" in an era, when others were performing the Halsted Radical mastectomy. He embarked upon a randomised controlled trial on pectoral node biopsy versus full axillary lymph node dissection way back in 1967 the so called "Cardiff Trial" and continued it in Edinburgh the "Edinburgh Trial". He is the author of many textbooks and monographs. He was the lead force behind the establishment of the national screening program on breast cancer in the UK.



Sir Patrick was the President of the Surgical Research Society and the Association of Surgeons of Great Britain and Ireland and a member of the Medical Subcommittee of University Grants Committee, Medical Research Council, Advisory Board for Research Councils, the Scientific Advisory Committee of the Cancer Research Campaign and the Council of the Royal College of Surgeons of Edinburgh. His achievements in the field of breast cancer earned him the Lister Medal by the Royal College of Surgeons of England in 1987. He chaired the Department of Health working group on the implementation of National Health Service Programme on nationwide breast cancer screening. His thinking on breast Screening was greatly influenced by Maureen Roberts who he had recruited to join his team in Cardiff.

He was ahead of his times, proposing a minimal access approach to axilla and perhaps the first surgeon to conceive the idea of "pectoral node biopsy later named axillary four node sampling" in an era, when others were performing the Halsted Radical mastectomy. He embarked upon a randomised controlled trial on pectoral node biopsy versus full axillary lymph node dissection way back in 1967 the so called "Cardiff Trial" and continued it in Edinburgh the "Edinburgh Trial". He is the author of many textbooks and monographs. He was the lead force behind the establishment of the national screening program on breast cancer in the UK.

- Forrest APM, Everington D, McDonald C. C., Steel R.J.C., Chetty U., Stewart H.J.(1995) The Edinburgh randomized trial of axillary sampling or clearance after mastectomy November <u>https://doi.org/10.1002/bjs.</u> <u>1800821118</u>
- Forrest, Patrick, Sir. (1986) Breast cancer screening: report to the Health Ministers of England, Wales, Scotland & Northern Ireland; Great Britain. Department of Health and Social Security. Published London: H.M.S.O.
- 3. Forrest APM (1990) Breast cancer: the decision to screen: Nuffield Trust ISBN 0900574747



Professor LE Hughes DS FRACS FRCS born in the village of Paramatta, Australia, in 1932 studied medicine in Sydney, Australia. After initial surgical training in Sydney, he moved to London for higher training at West Middlesex hospital. He was awarded British Empire cancer research campaign research fellowship to work at Kings College London in 1962–1963. Here he performed some basic research in the field of cancer immunology. He was appointed as a reader in surgery in Brisbane, Queensland. He received UICC Eleanor Roosevelt international cancer fellowship to work in Roswell Park Memorial Hospital in Buffalo, USA (1969–1970 where he worked with the famous plastic surgeon Dr VY Bakamjian). Prof Hughes joined Welsh National School of Medicine as the Chairman of the Department of Surgery in 1971, taking over from Sir Patrick Forrest. He retired in 1992.

He served as President of Surgical Research Society of Great Britain between 1991 and 1993. He also served as chairman of the editorial board for European Journal of Surgical Oncology 2000–2005. He was James the IV traveler awardee and Huntarian Professor Royal College of Surgeons 1987.



Prof Hughes was instrumental in starting several research projects and specialised care in various aspects of benign breast disease and breast cancer. He established a "mastalgia clinic", a "breast cyst clinic", a "dominant breast lump clinic" a general breast clinic and a chemotherapy clinic. He originated research and clinical work leading to the development of renowned concept of ANDI to explain the aetiopathogenesis of benign breast disease (BBD). The ANDI concept revolutionised the understanding and care of women suffering from various benign breast conditions. Prof Hughes collected all these studies to publish the first textbook dedicated to benign diseases with co-authors David Webster and Robert Mansel. This treatise in BBD, a masterpiece of medical literature, is revered as the "Bible of BBD".



Mitotic Clinic: The precursor of "multidisciplinary team (**MDT**) meeting: Long before the inception of MDT concept, he initiated combined modality approach for most cancers and conducted a regular weekly departmental mitotic meeting where all the cancer cases would be presented by a registrar, followed by a discussion with the team of oncologists from the

regional *Velindre Cancer Centre*. These mitotic meetings offered a great teaching and learning opportunity to trainees, as the diagnostic skills for lumps and skin lesions were honed and oncological principles of treatment were critically appraised.

He also developed his own technique of performing major mammary duct excision which is an advancement over the conventional Hadfield technique. He was one of the earliest surgeons in Britain to initiate immediate breast reconstruction after mastectomy. It is noteworthy that at his time, most surgeons would leave the breast reconstruction for plastic surgeons to perform about 6 months to 2 years after the initial treatment for breast cancer fearing an increased risk of recurrence hidden underneath a flap on the chest wall. This was the first initiative towards oncoplastic breast surgery by volume replacement. Many of his publications in 1980s' had advocacy for immediate breast reconstruction. He taught us that when a lady wakes up from anaesthesia following a mastectomy, she should not wake up with a flat chest, but have a rounded mound so that she is not reminded of her breast cancer. Because of his training with plastic surgeon Dr VY Bakamjian, he was adept in performing most of myocutaneous and fascio-cutaneous flap reconstructions himself. Prof Hughes trained a large number of surgeons from across the word and many surgeons of repute from the Indian subcontinent; Hari Shukla, VK Shukla and Ajay Khanna of BHU, Sandeep Kumar, Anurag Srivastava, Sunita Shrotria from Allahabad; Aravindan Nair of CMC-Vellore; BS Srinath of Bengaluru; and Ahmad from Thiruvananthapuram.

Prof Hughes (in the centre) visited India frequently. This picture is from his visit to Allahabad now Prayagraj, Uttar Pradesh (1979), where he was friends with Prof Pritam Das (extreme left), VB Sahai 2nd from left, Prof HS Shukla 2nd right and Prof CK Gupta extreme right

- Hughes LE, Mansel RE, Webster DJ. (1987) Aberrations of normal development and involution (ANDI): a new perspective on pathogenesis and nomenclature of benign breast disorders. Lancet. Dec 5; 2(8571):1316-9.
- Hughes LE, Mansel RE, Webster DJT, Sweetland HM. (2009) Hughes, Mansel & Webster's Benign Disorders and Diseases of the Breast. Ed 3. Philadelphia: Saunders.
- Mansel RE, Horgan K, Webster DJ, Shrotria S, Hughes LE. (1986) Cosmetic results of immediate breast reconstruction post-mastectomy: a follow-up study. *Br J Surg.* ;73(10):813–816
- Hughes LE. (1991) Classification of benign breast disorders. The ANDI classification based on physiological processes within the normal breast. *Br Med Bull.* ;47(2):251– 257



Professor Michael Baum MB ChB ChM MD born in 1937 did his medical education from Birmingham (MBChB 1960) and Fellow Royal College Surgeons in1965, ChM (Master of Surgery) in 1972, MD (hon) Gotenburg University 1986, Fellow of the Royal College of Radiology (hon) 1998 and Fellow Royal Society of Arts 1998-2004. He served as a senior lecturer and later reader in surgery, at the Welsh National School of Medicine between 1974 and 1979 in Cardiff. He became Professor of surgery in King's College London in 1980-1990. He served as the Director of Cancer Research Campaign between 1980 and 1995. He later moved to the Royal Marsden Hospital and Institute of Cancer Research as the Professor of Surgery (1990-1996) and to the University College London (UCL) between1996 and 2002. He started the first purpose-built clinical trial centre in 1980 and the first nurse counselling service at Kings College Hospital in 1981 and the first psychosocial oncology research team. He developed the first psychometric instrument for measuring quality of life in patients undergoing treatment for cancer (LASA). He now serves as Professor Emeritus of Surgery and visiting Professor of Medical Humanities at University College London. He was the first to demonstrate the benefit of adjuvant tamoxifen in early breast cancer. He started one of the largest international cancer trials ATAC-Arimidex, Tamoxifen, Alone or in Combination.

Prof Baum developed an innovative method of intraoperative radiotherapy for patients with early breast cancer, called TARGIT, which has recruited patients from the UK, Europe, Australasia and the USA. Prof Baum has been honoured by a large number of highly coveted awards, just to name a few: Skinner Medal, Royal College Radiologists; Gold Medal, International College of Surgeons; Ernest Miles Medal, Royal College of Surgeons; Celebrating Survival Award, San Antonio Breast Cancer Conference 2000; The William McGuire award, San Antonio, Texas 2002 (Annual award for a life-time achievement in breast cancer research); Best of Oncology, American Society Clinical Oncology 2002; Miami Breast Cancer conference award 2001; Best of Oncology, American Society Clinical Oncology 2002; St. Gallen award 2007,; and the Raven Award for lifetime achievement in Surgical Oncology, 2013.

- Baum M, Budzar AU, Cuzick J, Forbes J, Houghton JH, Klijn JG, Sahmoud T (2002) ATAC Trialists' Group. Anastrozole alone or in combination with tamoxifen versus tamoxifen alone for adjuvant treatment of postmenopausal women with early breast cancer: first results of the ATAC randomised trial. Lancet. Jun 22;359(9324):2131-9. doi: 10.1016/s0140-6736(02)09088-8. Erratum in: Lancet 2002 Nov 9;360(9344):1520.
- Cuzick J, Sestak I, Cawthorn S, Hamed H, Holli K, Howell A, Forbes JF. (2015) IBIS-I Investigators. Tamoxifen for prevention of breast cancer: extended long-term follow-up of the IBIS-I breast cancer prevention trial. Lancet Oncol. Jan;16(1):67-75. doi: 10.1016/S1470-2045(14)71171-4.
- Vaidya JS, Wenz F, Bulsara M, Tobias JS, Joseph DJ, Keshtgar M, Flyger HL, Massarut S, Alvarado M, Saunders C, Eiermann W, Metaxas M, Sperk E, Sütterlin M, Brown D, Esserman L, Roncadin M, Thompson A, Dewar JA, Holtveg HM, Pigorsch S, Falzon M, Harris E, Matthews A, Brew-Graves C, Potyka I, Corica T, Williams NR, Baum M (2014) TARGIT trialists' group. Riskadapted targeted intraoperative radiotherapy versus wholebreast radiotherapy for breast cancer: 5-year results for local control and overall survival from the TARGIT-A randomised trial. Lancet. Feb 15;383(9917):603-13. doi: 10.1016/S0140-6736(13)61950-9
- Mittra I, Baum M, Thornton H, Houghton J.(2000) Is clinical breast examination an acceptable alternative to mammographic screening? BMJ. Oct 28;321(7268):1071-3.



David JT Webster MD, FRCS, graduated from Bristol University. He was instrumental in introducing the

concept of immediate reconstruction in Great Britain. With Les Hughes, he developed the use of myocutaneous flaps for this purpose: initially latissimus dorsi and subsequently rectus abdominis. He performed the first immediate rectus abdominis breast reconstruction in Britain. He had earlier used this technique as a salvage procedure for a radio-necrotic ulcer on the chest wall. David continued to reassess the impact of immediate breast reconstruction both in terms of impact on survival and quality of life in detail for a long time.

His MD thesis was based on the effects of immunotherapy on the immune system work that was done in Cardiff and at the Ohio State University in Columbus as the JP Minton Research Fellow. He delivered the 1984 SN Mathur oration to the UP chapter of the Indian Surgical Association. He served as Visiting Professor of Surgery to the BP Koirala Institute of Health Sciences, Dharan Nepal. He was also an examiner for the FRCS and CME Tutor and advisor to CORESS for the Royal College of Surgeons of England.

He was an early investigator in the development of neoadjuvnt chemotherapy in the treatment of locally advanced breast cancer. He was involved in numerous National Clinical Trials of breast cancer treatment related to hormonal manipulation while continuing a laboratory research programme related to T-cell function. He was closely involved with many clinical trials of mastalgia and breast cysts. He initiated a follow-up analysis of Wolfe's mammographic patterns to see how they changed over time. His deep sense of commitment and dedication towards medical education won him the prestigious position of **Clinical Dean** at the University of Wales, College of Medicine, Cardiff.

David Webster served as a major contributor to the three editions of the book on benign breast disease, the best in-depth treatise on benign breast disease. He stated that he would hope to be remembered as a **sound clinician** who did his best for his patients, who tried to advance our understanding of breast cancer and who did his best to promote and excite the trainees towards excellence.

- Webster DJT, Chare MJB, Baum M. The effect of intravenous corynebacterium parvum on an immune profile of women with breast cancer. Developments in Biological Standards 38 467-470 1978
- Webster et al Immediate reconstruction of the breast after mastectomy. Is it safe? Cancer 53; 1416-1419: 1984
- 3. Webster DJT, Cornacoff JB, Vallera DA, Dalmasso JP, Dodd MC, Minton JP. Immune RNA therapy of a murine sarcoma. Journal of Surgical Oncology 12 213-220 1979

- Patel RT, Webster DJT, Mansel RE, Hughes LE. Is immediate post mastectomy reconstruction safe in the long term? European Journal of Surgical Oncology 19, 372-375, 1993
- 5. McClaren DB, Morrey DM, Keen CW, Webster DJT, Barrett-Lee PJ. Fifteen years of primary chemotherapy for locally advanced inoperable carcinoma of the breast. The Breast 1997; 6: 266-270
- Hughes LE, Mansel RE, Webster DJT.(2009) Benign diseases and disorders of the breast: concepts and clinical management. Balliere Tindall, London 1989 .Ibid, 3rd Edition, Mansel RE, Webster DJT, Sweetland HM ELSEVIER



Prof Hari S Shukla MS FRCS PhD DSc graduated in medicine from the University of Allahabad in 1967 and joined the Army Medical Corps (AMC) in 1968. He served as a Captain in AMC during the Bangladesh freedom war in 1971. He later joined University of Allahabad for surgical training under the famous teacher of teachers, Prof Pritam Das, and was awarded Master in Surgery in 1974 with a gold medal. He was invited in January 1975 to work with Prof LE Hughes in Cardiff as a registrar and later as a senior lecturer at the Welsh National School of Medicine. He took great interest in surgical research in general and cancer immunology in particular-an interest that he continued on his return to his alma mater in Allahabad and conducted several research projects related to immune functions in surgical and gynaecological patients and measures to improve the immune parameters with adequate nutritional supplementation. He trained a

large number of breast surgeons both in Cardiff and in Allahabad and Varanasi. He was offered a lecturer's post in the world renowned Benaras Hindu University (BHU), Department of Surgery. He very soon escalated to the level of professor and later the first Chair in the Surgical Oncology in the Northern India. He was instrumental in setting up the dedicated Department of Surgical Oncology at BHU where he served as the founder chief till his retirement. His profound contribution to the research and training in surgical oncology enabled him to decorate the Presidentship of the World Federation of Surgical Oncology Societies and the Indian Society of Surgical Oncology. Dr HS Shukla created a very active silent movement for setting up a Cancer Hospital in BHU from 1990 onwards. The result of this effort was the creation of the Division of Surgical Oncology that was raised to be the Department of Surgical Oncology in a few years. His efforts for a BHU Cancer Hospital also succeeded in the form of Homi Bhabha Cancer Hospital and Mahamana Pt. Madam Mohan Malaviya cancer centre in BHU (now being managed by Tata Memorial Centre). Thus, he succeeded in being instrumental in the establishment of a comprehensive cancer management system in Varanasi.

Dr HS Shukla has maintained a continuous academic and physical contact with Cardiff for over 40 years with a sustained flow of knowledge and many bright brains from Orient to Wales. He was instrumental in providing training to a large number of young Indian surgeons in Cardiff (Sandeep Kumar, Anurag Srivastava, Sunita Shrotria, Ajay Khanna, VK Shukla, Sanjeev Gupta).

His academic accolades won him the prestigious position of Dean of Institute of Medical Sciences at BHU. Following his retirement, he was honoured the Emeritus Professorship and later Distinguished Professorship in BHU. He is a surgical scholar of wide erudition and profound knowledge. Watching him operate gives the pleasure of reading a poetry of Wordsworth, Shakespeare or Rabindranath Tagore. Most breast surgeons in India have directly or indirectly been influenced by his magnetic personality, magical surgical skills and fathomless knowledge.

- Shukla HS, Hughes LE, Whitehead RH, Newcombe RG. Long-term (5-11 years) follow-up of general immune competence in breast cancer.(1986) I. Pre-treatment levels with reference to micrometastasis. Cancer Immunol Immunother. ;21(1):1-5.
- Shukla HS, Melhuish J, Mansel RE, Hughes LE. (1999) Does Local Therapy affect Survival rates in Breast Cancer?. Anns Surg Oncol. 6(5): 455-460.
- Shukla HS, Kumar S. (1989) Benign breast disorders in nonwestern populations: Part II-Benign breast disorders in India. World J Surg. Nov-Dec;13(6):746-9.



Prof Robert E Mansel CBE MS FRCS is famous for his work on benign breast disease in general and mastalgia in particular. He is perhaps one person who has conducted maximum number of randomised trials and studies in treatment of mastalgia. Prof Mansel has contributed immensely in improving the quality of care of women with both benign and malignant breast disease, by generating highest quality of Level One Evidence in the field of breast diseases in general and sentinel node biopsy in particular. He served as the President of European Society of Mastology (EUSOMA), the largest body of professionals engaged in basic and clinical research and quality improvement across the breast care centres within Europe. He has made a significant contribution in setting the quality indicators and rigorous audit of European breast cancer centres.

Main contributions of Prof Mansel in the arena of breast cancer care are as follows:

Professor Robert E Mansel won a scholarship from the *UICC* and *WHO* to work with Dr **WilliamMcGuire** in **San Antonio** in 1982–1983 on oestrogen receptor (ER) study using an antibody to ER. He was the first UK fellow in Bill's lab and worked alongside George Sledge. This experience provided a lifelong stimulus to devote his time to clinical research and equipped him to successfully win several coveted research grants. On returning to the UK, he set up a research program looking at many aspects of the biology and surgery of breast cancer with a view to de-escalating the extent of surgical therapy for breast cancer. He focused on the developing field of sentinel node biopsy and obtained funding from

the Medical Research Council UK, to carry out the first multicentre randomised trial in the UK which enrolled over 1000 patients as the PI of the ALMANAC Trial. The results of the ALMANAC Trial were presented at the San Antonio symposium and published in JNCI. Following on from his trial, he obtained funding from the Government of United Kingdom for a unique training program for the whole UK to standardised high-quality training to UK surgeons (THE NEW START training program). This ensured that all the breast surgeons were rapidly trained to a high quality and were able to rapidly institute the new technique in their hospitals. In recognition of this service, he was honoured by Her Majesty Queen Elizabeth II with the award of the Commander of the Order of the British Empire (CBE), the second highest-ranking order of the British Empire award (excluding knighthood and Damehood).

As the training program had produced a cohort of validated trained surgeons, this allowed the NEW START team of British surgeons to enter directly into the AMAROS trial (After Mapping Of The Axilla: Radiotherapy Or Surgery) without needing preliminary quality assurance required by the European surgeons and Prof Mansel became the PI for the UK and entered many patients. The success of this trial is well known and has been presented on several occasions in the San Antonio symposium. He has been a major participant in the IBIS- I and IBIS -II (International Breast cancer Intervention Study) prevention trials and is currently chairing the steering committee of the LORIS trial. Owing to his enormous contribution in breast cancer care, he was elected as the president of European Society of Mastology (EUSOMA) in 2014 and continued till 2017. As EUSOMA president, he devoted significant time to quality assurance among European breast units in order to ensure high-quality care for breast cancer patients in Europe. He is currently chairing a 6-year program of guidelines and quality assurance on behalf of the European Commission which is continuing despite Brexit as he has been appointed for his experience and leadership in Europe. He remains active in basic research even at age 72 years. His group has filed a patent looking at novel methods of percutaneous nonsurgical ablation of screendetected cancers in order to explore the de-escalation of primary excisional surgery for breast cancer. He has trained a large number of breast surgeons within the UK, Europe and India. Some of his trainees serve as chief of surgery/director in the leading medical institutes and as the president of the breast societies in India. He has conducted many training courses and operative workshops in centres of excellence, like All India Institute of Medical Sciences, New Delhi;

Banaras Hindu University, Varanasi; and King Georges Medical College, Lucknow, India. He will receive the Raven lifetime achievement award from the British Association of Surgical Oncology (BASO) this year.



Sandeep Kumar (left), Hari Shukla (centre) and Robert Mansel (right) at the Taj Agra 2017

- Hughes LE, Mansel RE, Webster DJ. (1987) Aberrations of normal development and involution (ANDI): a new perspective on pathogenesis and nomenclature of benign breast disorders. Lancet. Dec 5;2(8571):1316-9.
- Mansel RE, Fallowfield L, Kissin M, Goyal A, Newcombe RG, Dixon JM, Yiangou C, Horgan K, Bundred N, Monypenny I, England D, Sibbering M, Abdullah TI, Barr L, Chetty U, Sinnett DH, Fleissig A, Clarke D, Ell PJ.(2006) Randomized multicenter trial of sentinel node biopsy versus standard axillary treatment in operable breast cancer: the ALMANAC Trial. J Natl Cancer Inst. May 3;98(9):599-609.
- 3. Donker M, van Tienhoven G, Straver ME, Meijnen P, van de Velde CJ, Mansel RE, Cataliotti L, Westenberg AH, Klinkenbijl JH, Orzalesi L, Bouma WH, van der Mijle HC, Nieuwenhuijzen GA, Veltkamp SC, Slaets L, Duez NJ, de Graaf PW, van Dalen T, Marinelli A, Rijna H, Snoj M, Bundred NJ, Merkus JW, Belkacemi Y, Petignat P, Schinagl DA, Coens C, Messina CG, Bogaerts J, Rutgers EJ.(2014) Radiotherapy or surgery of the axilla after a positive sentinel node in breast cancer (EORTC 10981-22023 AMAROS): a randomised, multicentre, open-label, phase 3 non-inferiority trial. Lancet Oncol. Nov;15(12):1303-10
- 4. Mansel RE, Goyal A, Preece P, Leinster S, Maddox PR, Gateley C, Kubista E, von Fournier D. (2004) European randomized, multicenter study of goserelin (Zoladex) in the management of mastalgia. Am J Obstet Gynecol. Dec;191(6):1942-9.
- Srivastava A, Mansel RE, Arvind N, Prasad K, Dhar A, Chabra A. (2007) Evidence-based management of Mastalgia: a meta-analysis of randomised trials. Breast. Oct;16(5):503-12



Prof Sandeep Kumar MS FRCS PhD MMSc ex-professor of surgery, King George's Medical University, Lucknow and Founder Director, All India Institute of Medical Sciences, Bhopal. He is an alumnus of the University of Allahabad. He joined the University Hospital of Wales, Department of Surgery, in 1981. He was awarded FRCS from the Royal College of Surgeons of Edinburgh and PhD from the University of Cardiff, Wales, with Prof Robert Mansel as his mentor. He was awarded Rockefeller INCLEN fellowship in 1990 to visit Newcastle, Australia, where he accomplished an advanced course in clinical epidemiology and was awarded a master's degree, MMsc, in Clinical Epidemiology and Research Methodology.

He was a visiting fellow in Freiberg, Germany, Sloan Kettering Cancer Institute, New York, and University of New South Wales, Australia. He is the past editor, secretary and president of the Indian Association of Surgical Oncology and Chairman of Research Grants Committee, Indiaclen. He is scientific advisor and research grants review group member of Indian Council of Medical Research (ICMR). He conducted over 10 major research projects in cancer biology and epidemiology as PI. He has been the team leader in a collaborative research with the University of Minnesota. He worked extensively at the famous Cardiff Breast Clinic. He is editor-in-chief of Indian Journal of Surgery. He received National Medical Sciences Academy award for evolving modern concept of benign breast disorders and its endocrinological background and treatment. His research in mastalgia turns a full circle from documenting natural history to aetiopathogenesis, clinical classification and nomenclature, epidemiology of breast pain and nodularity, and creation of an objective instrument to record breast nodularity and effective, harmless, inexpensive treatment of mastalgia. This work won him the **national award**— National Academy of Medical Sciences of India award. A brief description of his contribution is given below.

Breast pain or mastalgia often associated with nondiscrete lumpiness of the breast was erroneously interpreted as a histo-morphological disease for several decades. A sounding board article in New England Journal of Medicine declared fibrocystic breast disease a non-disease. He first described the natural history of breast pain and the clinical classification of benign breast disorder (BBD). He unfolded the subtle endocrinological perturbations in BBD through a series of experiments conducted by him. This was followed by populationbased epidemiology of breast pain and nodularity, development of an objective tool for assessment of breast pain and nodularity and a double-blind randomised placebo controlled clinical trial to successfully treat breast pain and nodularity.

Histo-morphological basis of BBD: Breasts are composed of epithelial system of ducts and lobulo-alveolar secretary units embedded in adipose tissue with interspersed fibrous septae derived from mesenchymal tissue. The growth and morpho-genesis of these tissues occur in various stages associated with concurrent hormonal changes in the female body. Such changes are also affected by genetic constitution and mutation. Breast growth secretion and involution are affected by systemic hormones, the sensitivity of its glandular and stromal tissue to the circulating hormones and the milieu interior of its paracrine effects of locally derived factors affecting the epithelium and stromal relationship. This forms the major basis of benign breast disorders mainly breast pain and nodularity. Its histo-pathogenesis was erroneously described by previous authors.

Natural history of mastalgia: An untreated cohort of 258 patients with cyclical breast pain was followed for 7 years, and the natural history was described for the first time. Two distinct pain patterns were identified, i.e., cyclical pronounced mastalgia (CPM) and non-cyclical mastalgia (NCM). Two populations emerged: one experience relief after a mean of 3 years, and in another the pain was persistent for up to two decades. The cyclical pain generally related to a hormonal event, started early in life and usually abated at menopause

spontaneously. This study indicated that type of pain and age at onset may allow some prediction of the course of disease and choice of therapy.

Epidemiology: With social, economic, educational and information evolution increasing number of women solicit medical opinion for pain and nodularity in breasts but unfortunately majority are poorly managed and unnecessary biopsies and cancer phobia is commonly generated. If it is mild, it can be regarded as normal. This condition was described as **ANDI or aberration of normal development and involution**. It has no histological basis. Breast nodularity is a physiologic, hormonally mediated change characterised by lumpiness of the breast and varying degrees of pain and tenderness. Its prevalence in the community and hospital-based population was described.

Actiology of mastalgia and nodularity-ANDI: In the past, benign breast disease for most doctors has been regarded as synonymous with "fibroadenosis" or "fibrocystic disease". These terms were used for the syndrome of premenstrual pain and nodularity. This concept arose from the unfortunate fact that early workers described histological changes of fibrosis, adenosis, cyst formation and apocrine metaplasia and assumed a causative association. Subsequently, it was well established that these histological changes were normal features of the breast microanatomy and ubiquitous in nature. Three main theories have emerged regarding the aetiology of painful nodular breasts: (1) increased oestrogen secretion from the ovary, (2) deficient progesterone production (or "relative hyperoestrogenism") and (3) hyper-prolactinaemia. In summary, pulsatile secretion of prolactin and/or gonadotropins is abnormal in painful nodular breasts. The serum levels of oestrogen, the administration of which is known to cause symptoms of painful nodularity, do not seem to be abnormal in patients with cyclical mastalgia. The progesterone deficiency due to inadequate corpus luteal function is unlikely to be present. Ironically, a defect in the tissue response or an end organ abnormality has not been investigated so far.

Lucknow Cardiff breast nodularity scale was developed: The Breast nodularity scale is a 5-point ordinal scale depicting increasing order of nodularity in the breast. Clinically breast nodularity is most commonly noticeable in the upper outer quadrant of the breast that has the maximum amount of breast tissue, hence the depiction of a scheme mostly shown in the upper outer quadrants of the breasts. Grade 0 depicts a smooth textured breast with extreme extent of normalcy and grade 4 the maximum nodularity. In the present scale, the five figures are cue for the examining doctor to chart the nodularity in the index breast. The examining clinician or nurse is taught to make a holistic interpretation of breast nodularity as a sum of area or quadrants involved and the coarseness of nodularity. Approximately, two thirds of normal women have some grade of nodularity.

Treatment of mastalgia: There was a need to find a drug for mastalgia which is effective and safe. Several agents have been tried. The two broad categories used are hormonal and non-hormonal. Hormonal manipulation is done by danazol, tamoxifen, bromocriptine, progesterone, oral contraceptive pill and more recently LHRH analogue or goserelin or GLA-gamma linolenic acid. Non-hormonal agents include analgesics (oral/topical), plant extracts like fructus-agni-casti, evening primrose oil and GLA. Double-blind randomised placebocontrolled clinical trial of oral centchroman 30 mg (ormeloxifene) and a SERM or placebo twice a week for 3 months in women (20-50 years) with pronounced breast pain with or without lumpiness were recruited after excluding discrete benign lump or cancer. Serial assessments of pain on a visual analogue scale and nodularity grade on a 5-point ordinal Lucknow-Cardiff scale were done. A total of 151 patients were randomly allocated to two interventions using blocks of size four. Participants and physicians were blinded to randomization. Of the 151 patients, 121 (active = 57, placebo = 64) were available for efficacy analysis. The mean pain level showed a systematic downward trend over five visits (F = 105.23, p < 0.0001) that significantly reduced in active group compared with placebo (F = 18.66, p < 0.0001). The patterns of variation in pain over time for the individual groups differ from the overall mean pattern for two groups and thus from one another (F = 44.43, p <0.0001). Cumulative frequencies of breast nodularity grades during the successive visits showed significant improvement (p = 0.001) compared with placebo at the end of third month. The effect of active drug persisted till the completion (6 months) of the treatment (p <0.001). At the last visit, 93.3% of subjects in active group had grade 2 or lower nodularity as compared with 71.05% in the placebo. Oligomenorrhea alone was reported in 12 subjects. Centchroman showed significant efficacy for treating breast pain and nodularity.

- Kataria K, Dhar A, Srivastava A, Kumar S, Goyal A . (2013) A systematic review of current understanding and management of mastalgia.. Indian J Surg 2013; 75: 1-6 (DOI 10.1007/s12262-013-0813-8)
- 2. Wisbey JR, Kumar Sandeep, Mansel RE, Preece PE, Pye JK, Hughes LE. (1983) Natural history of breast pain. Lancet ; ii: 672-74

- 3. Kumar Sandeep(1984) Studies on the role of prolactin in the aetiology of breast disease. University of Wales College of Medicine PhD Thesis
- Kumar Sandeep, Mansel RE, Scanlon MF, Hughes LE, Edward CA, Woodhead JS, Newcombe RG.(1984) Altered responses of prolactin, luteinizing hormone and follicle stimulating hormone secretion to thyrotropin releasing hormone gonadotrophin releasing hormone stimulation in cyclical mastalgia. Br J Surg ; 71: 870 – 873
- Kumar Sandeep, Mansel RE, Hughes LE. (1983) Secretory response of prolactin and TSH in benign breast disease before and after TRH stimulation. Br J Surg (abstract); 70: 293
- Kumar Sandeep, Mansel RE, Hughes LE, Woodhead JS, Edwards CA, Scanlon MF, Newcombe RG. (1984) Prolactin response to thyrotropin-releasing hormone stimulation and dopaminergic inhibition in benign breast disease. Cancer; 53:1311-15
- Kumar Sandeep, Mansel RE (1984) Prolactin and antiemetics for adjuvant chemotherapy of breast cancer.. Br Med J 1984; 288: 760
- Kumar Sandeep, Mansel RE, Scanlon MF, Hughes LE, Edwards CA, Woodhead JS and Newcombe RG.(1984) Altered responses of prolactin, luteinizing hormone and follicle stimulating hormone secretion to thyrotropin releasing hormone/ gonadotrophin releasing hormone stimulation in cyclical mastalgia. Br J Surg ; 71:870-73
- 9. Kumar Sandeep, Mansel RE, Hughes LE, Edwards CA and Scanlon MF (1985) Prediction of response to endocrine therapy in pronounced cyclical mastalgia using dynamic tests of Prolactin release. . Clin Endocrinal (Oxford) 1985; 23: 699-704
- Kumar Sandeep, Mansel RE, Read GF, Truran PL, Wilson DW and Hughes LE. Br J Surg (1986) Daily salivary progesterone levels in cyclical mastalgia patients and their controls. ; 73: 260 – 263 Presence and possible significance of immunohistochemically demonstrable prolactin in breast apocrine metaplasia. Kumar Sandeep, Mansel RE, Jasani B. Br J Cancer 1987; 55: 307-309
- Agarwal PK, Tandon S, Agarwal AK, Kumar Sandeep (1989) Highly specific sites of prolactin binding in benign and malignant breast tissue., Ind J Exp Biol ; 27: 1035-1038
- 12. Shukla HS, Kumar Sandeep. (1989). Benign breast disorders in NonWestern populations: Part II benign breast disorders in India. World J Surg ; 13: 747
- Kumar Sandeep, Rai R, Das V, Dwivedi V, Kumar S, Agrawal GG. (2010). Visual analogue scale for assessing breast nodularity in non-discrete lumpy

breasts: The Lucknow Cardiff breast nodularity scale. The Breast ; 19: 238 - 242

 Kumar Sandeep, Rai R, Agarwal GG, Dwivedi V, Kumar S, Das V. (2013) . A randomised double-blind placebo controlled clinical trial of Centchroman (Ormeloxifene) in breast pain and nodularity (Benign Breast Disorder). Nat Med J India ; 26: 69-74



Prof Anurag Srivastava MS FRCS PhD MPH received his training in Cardiff during the period from March 1983 to March 1988. He worked very closely with Prof. Hughes, David Webster, HS Shukla and Robert Mansel. He took part in various research projects on benign breast diseases and breast cancer being undertaken in the department. He performed evaluation of tumour-induced angiogenesis in skin cancers and breast cancer. He was awarded a research fellowship from Cancer Research Campaign UK and completed a thesis on tumourinduced angiogenesis for which he was awarded PhD by the University of Wales, Cardiff, in 1987. His work produced the first clinical evidence that metastasis in cancer is dependent on tumour neovascularization. He returned to India in 1988 and worked initially under supervision of Prof. H.S. Shukla at BHU Varanasi and later at the All India Institute of Medical Sciences, New Delhi. He served

AIIMS for 31 years and retired as chairman of the department of surgery in December 2020. He conducted a large number of randomised trials and started some of the first studies in the field of both benign disease and in breast cancer, just to name a few: the first trial, assessing the benefit of centchroman in mastalgia; the trial on evaluating oncoplasty versus simple closer for breast conserving surgery; first trial of fluorescein versus radioisotope in sentinel node mapping in breast cancer; randomised controlled trial on extent of milk duct excision in periductal mastitis; and first decision analysis approach on nonlactational mastitis.

Working closely with Dr. Sudhir Gupta at the Directorate General of Health Services (NCD) at the Ministry of Health and Family Welfare; Dr. JS Thakur of the School of Public Health, Postgraduate Institute of Medical Education and Research (PGIMER-Chandigargh); and Dr. Ravi Mehrotra, director of the National Institute of Cancer Prevention and Research (ICMR), he persuaded the government to launch the National Cancer Screening in India on a model of "Multidisease screening for Non-communicable diseases (NCD)" by the Ministry of Health and Family Welfare, Government of India. He remains active as an instructor to medical officers and nurses for the National Cancer Screening. He initiated the first MCh programme on breast and endocrine surgery in AIIMS, New Delhi. He contributed to the chapter on "The Breast" in "Bailey & Love's Short Practice of Surgery 28th Edition (in press)".

- Srivastava A, Mansel RE, Arvind N, Prasad K, Dhar A, Chabra A.(2007) Evidence-based management of Mastalgia: a meta-analysis of randomised trials. Breast. Oct;16(5):503-12.
- Dhar A, Srivastava A. (2007) Role of centchroman in regression of mastalgia and fibroadenoma. World J Surg. Jun;31(6):1178-84
- Tejwani PL, Srivastava A, Nerkar H, Dhar A, Hari S, Thulkar S, Chumber S, Kumar S. (2011) Centchroman regresses mastalgia: a randomized comparison with danazol. Indian J Surg. Jun;73(3):199-205
- Rajaraman P, Anderson B O, Basu P, Belinson J L, D' Cruz A, Dhillon P K, Gupta P, Jawahar T S, Joshi N, Kailash U, Kapambwe S, Katoch, V M, Krishnan S, Panda D, Sankaranarayanan R, SelvamJ M, Shah KV, Shastri S, Shridhar K, Siddiqi M, Sivaram S, Seth T, Srivastava A, Trimble E, Mehrotra R,(2015) "Recommendations for screening and early detection of common cancers in India", The Lancet Oncology, Vol.16(7), July 352-361.
- Pathania S, Khan MI, Kumar A, Gupta AK, Rani K, Ramesh Parashar T, Jayaram J, Ranjan Mishra P, Srivastava A, Mathur S, Hari S, Hariprasad G. (2020)

Proteomics of sentinel lymph nodes in early breast cancer for identification of thymidylate synthase as a potential biomarker to flag metastasis: a preliminary study. Cancer Manag Res. 2020 Jun 23;12:4841-4854

- Badwe RA, Kataria K, Srivastava A. (2013) Surgical resection of phyllodes tumour: a radical approach as a safeguard against local recurrence. Indian Journal of Surgery. Published Online June, DOI- 10.1007/s12262-013-0935-z. Online ISSN 0973-9793.
- Srivastava A, Badwe RA, Prem A, Parmar V, Seenu V, Dhar A, et al.(2015) Abstract P2-01-31: Sentinel node mapping with fluorescein and comparison with methylene blue and technitium sulphur colloid in early breast cancer. Cancer Res. May 1; 75(9 Supplement): P2-1-31-P2-01–31



Amit Goyal, MS, MD, FRCS, practices as a Consultant Oncoplastic Breast Surgeon and associate professor at the University Hospitals of Derby and Burton NHS Foundation Trust, UK, and is the Clinical Lead for Breast Surgery. Amit studied medicine (MBBS) and received his medical education at the premier medical institute, the All India Institute of Medical Sciences, New Delhi. After completing his surgical training (MS) with Anurag Srivastava at AIIMS, he moved to Great Britain and joined Professor Robert Mansel's unit as a research fellow in Cardiff University in 2002 and later became a Clinical Lecturer in Surgery in 2004. He contributed to the ALMANAC trial and NEW START sentinel node biopsy training program that firmly established sentinel node biopsy as the preferred method for axillary staging in early-stage breast cancer in the UK. He moved to Derby in 2011, where he has established a research program, focused on axillary management in breast cancer and breast reconstruction. He is the Oncology and Breast Specialty Editor of the Surgery journal (UK). He is the chief investigator of the largest UK led breast cancer surgical trials addressing the role of axillary treatment— POSNOC and ATNEC—and the BIOSYM randomised trial comparing synthetic meshes with biological matrices in women undergoing one-stage implant-based breast reconstruction.

There is uncertainty around the axillary management of patients with 1 or 2 nodal macro-metastasis. ACOSOG-Z0011 (Z11) showed that axillary node clearance (ANC) may be omitted in women with ≤ 2 positive nodes undergoing breast conserving surgery (BCS) and whole breast RT. However, the study had various limitations, and a confirmatory study is needed to clarify the role of axillary treatment in women with ≤ 2 macro-metastasis undergoing BCS and groups that were not included in Z11, e.g., mastectomy and those with microscopic extranodal invasion. POSNOC is a pragmatic, randomised, multicentre, non-inferiority, international (UK, Australia and New Zealand) trial in which participants are randomised in a 1:1 ratio (ClinicalTrials.gov: NCT02401685). Study includes women with T1/T2, unifocal or multifocal invasive breast cancer, and one or two nodes with macro- metastasis at sentinel node biopsy, with or without extranodal extension. The primary objective of POSNOC is to evaluate whether adjuvant therapy alone is non-inferior to adjuvant therapy plus axillary treatment, in terms of axillary recurrence within 5 years in women with 1 or 2 macro-metastases. The study has successfully completed planned recruitment of 1900 patients. The strengths of the study are as follows: sample size is more than twice compared with Z11 (1900 vs. 856), it includes mastectomy patients, and it has an inbuilt radiotherapy quality assurance programme coordinated by National Radiotherapy Trials QA (RTTQA) group and only patients with macro-metastases are eligible (unlike Z11 that included micro-metastasis). Neoadjuvant chemotherapy (NACT) downstages the axilla. Among patients with biopsy-proven axillary node metastases, contemporary treatment regimens yield axillary complete response rates of 40% or more. We have now learnt that sentinel node biopsy following neoadjuvant therapy in these patients has a false-negative rate of less than 5% if the preneoadjuvant treatment marked involved node is removed along with sentinel nodes. The node can be marked using special markers, e.g., placing a radioactive iodine seed, magnetic seed (Magseed), reflector (radar technology,

SAVI Scout®) or radiofrequency tag (LOCalizerTM) to mark the node. However, these techniques are costly and require a probe that costs more than 1 lakh rupees, apart from more than Rs 10,000 per patient cost for the implant. He has studied and refined the carbon dye technique that has the advantage of low cost and absence of need for special equipment. This technique will particularly be useful in countries with limited resources. He recently published the multicentre, feasibility study of carbon dye tattooing to mark the biopsied axillary node and surgical localisation in breast cancer patients. The results of the study have helped to refine the technique and develop a standardised protocol that can be adopted by other sites. The study recommends that 0.2-0.4 ml of black dye is injected in the cortex at the time of FNA or core biopsy or after the biopsy results at a separate visit (both approaches are feasible as shown in this study). Alternatively, to reduce the risk of diffusion of the dye into surrounding tissues with time, a clip can be placed in the involved node before NACT, and the clipped node/clip can be tattooed before surgery for identification intra-operatively. The surgeon can stop after confirming removal of clip on specimen x-ray in case of multiple black nodes. This technique can be used in other settings such as to mark the non-palpable node in patients undergoing excision biopsy of the axillary lymph node. For patients who are node positive to start at presentation and are found to have a complete nodal tumour response post-NACT (ypN0), we do not yet know whether local axillary therapy can be modified based on the response to neoadjuvant therapy. ATNEC randomised trial specifically addresses axillary management following neoadjuvant chemotherapy in patients with proven axillary node metastases. In ATNEC, patients receive neoadjuvant chemotherapy followed by sentinel lymph node biopsy. If the sentinel nodes have converted to benign, ATNEC (ClinicalTrials.gov: NCT04109079) randomly assigns patients to axillary treatment (nodal radiotherapy or axillary nodal clearance) vs no axillary treatment (without further surgery). This trial will give us a more definitive answer as to the long-term safety of sentinel node biopsy after neoadjuvant chemotherapy and whether we can modify local therapy based on the response to neoadjuvant chemotherapy. The primary outcomes are disease-free survival (DFS) and the risk of lymphoedema at 5 years. The study started recruitment earlier this year and the target sample size is 1900. He has contributed to the advancement of breast reconstructive surgery by describing the "halter-neck" modification of the inferiorly based dermal flap technique to perform pre-pectoral (above muscle) implant based one-stage or two-stage

breast reconstruction by saving the de-epithelialised areolar skin.

- Goyal A, Newcombe RG, Chhabra A, Mansel RE. (2006) ALMANAC Trialists Group. Factors affecting failed localisation and false-negative rates of sentinel node biopsy in breast cancer–results of the ALMANAC validation phase. Breast Cancer Res Treat. Sep;99(2):203-8
- Goyal A, Wu JM, Chandran VP, Reed MW (2011). Outcome after autologous dermal sling-assisted immediate breast reconstruction. Br J Surg 2011; 98(9): 1267-72
- Mansel RE, MacNeill F, Horgan K, Goyal A, Britten A, Townson J, Clarke D, Newcombe R, Keshtgar M, Kissin M, Layer G, Hilson A, Ell P, Wishart G, Brown D, West N. (2013) Results of a national training programme in sentinel lymph node biopsy for breast cancer. Br J Surg. 100(5):654-61
- 4. Goyal A. (2014). Protocol 14PRT/0519:POSNOC -Positive sentinel node-adjuvant therapy alone versus adjuvant therapy plus clearance or axillary radiotherapy: a randomised controlled trial of axillary treatment in women with early stage breast cancer who have metastases in one or two sentinel nodes (ISRCTN54765244). https://www.thelancet.com/ protocol-reviews/14PRT-0519
- Wheat JS, Choppin S, Goyal A (2014). Development and assessment of a Microsoft Kinect based system for imaging the breast in three dimensions. Med Eng Phys. 2014; 36(6):732-8
- Goyal A, Dodwell D. (2015) POSNOC: (2015) A randomised trial looking at axillary treatment in women with one or two sentinel nodes with macrometastases. Clin Oncol (R Coll Radiol). Dec;27(12):692-5
- Goyal A, Mann B, Thompson AM. (2019) Undissected axilla and axillary radiotherapy. JAMA Oncol. May 1;5(5):741-742
- Iqbal J, Goyal A. (2019). Halter neck extension of dermal flap for pre-pectoral breast reconstruction.10.13140/ RG.2.2.19166.97601
- Goyal A, Puri S, Marshall A, Valassiadou K, Hoosein MM, Carmichael AR, Erdelyi G, Sharma N, Dunn J, York J. (2021) A multicentre prospective feasibility study of carbon dye tattooing of biopsied axillary node and surgical localisation in breast cancer patients. Breast Cancer Res Treat. Jan;185(2):433-440.
- Goyal A, Cramp S, Wheatley D, Marshall A, Puri S, Homer T, Vale L, Mir R, Nabi Z, Rose J, Edwards HT, Ahmed S, Shaaban A, Elsberger B, Bruce J, Gasson S, Speirs V, Shaw J, Higgins H, Dunn J.

Axillary management in T1-3N1M0 breast cancer patients with needle biopsy proven nodal metastases at presentation after neoadjuvant chemotherapy - ATNEC (ClinicalTrials.gov NCT04109079) [abstract]. In: Proceedings of the 2020 San Antonio Breast Cancer Virtual Symposium; 2020 Dec 8-11; San Antonio, TX. Philadelphia (PA): AACR; Cancer Res 2021;81(4 Suppl):Abstract nr OT-04-01



Dr Raghu Ram Pillarisetti

OBE, MS FRCS (Eng), FRCS (Edin), FRCS (Glasg), FRCS (Irel), FACS, Hon. FRCS (Thailand), Hon FCSSL (Sri Lanka), Hon FCCS (China)

Dr Raghu Ram stated "My heartfelt appreciation for putting together this article to commemorate the legacy of Cardiff Breast Unit. Cardiff will forever be etched in my memory for two reasons. **Firstly**, my very first training post after obtaining FRCS was with Prof Robert Mansel, who was the Chief of Surgery & Head of Cardiff Breast Unit at the University Hospital of Wales. I also had the good fortune of completing six years of structured Higher Surgical Training in the all Wales Higher Surgical Training Programme when Prof Mansel was the Programme Director. Working with Prof Mansel inspired me to take up Breast Surgery as a career. **Secondly**, my mother was diagnosed with breast cancer whilst I was working in Wales & she underwent treatment for the same in Cardiff. This was a major turning point in my life. I relocated to India in 2007 to take care of my mother, and equally, strived to replicate the best of British practices by working alongside passionate colleagues and a proactive Government in an earnest endeavour to improve the delivery of breast healthcare in my motherland. My 'living bridge' reflection between the UK and India is detailed in the Editorial published in this Special issue of Indian Journal of Surgery".

Dr. Raghu Ram Pillarisetti is the founding director of KIMS-USHALAKSHMI Centre for Breast Diseases, Hyderabad (India), and the founder and CEO/director of Ushalakshmi Breast Cancer Foundation-a "not for profit" Breast Cancer Charity-which has championed a one of its kind breast cancer awareness drive ("The Pink Ribbon Campaign") in the southern Indian States of Telangana and Andhra Pradesh. The Royal College of Surgeons of Edinburgh conferred him with International Gold Medal (2013), which is the highest recognition bestowed upon fellows of the college practicing outside the UK, and he is the youngest ever recipient of this impressive award in the 516 years history of the college. He delivered the Col. Pandalai Oration, which is the highest academic honour bestowed by The Association of Surgeons of India (2018). He is one of the youngest surgeons to have served as President of Association of Surgeons of India (2020) and is widely recognised for his "creative leadership and accountable governance". He was the principal driving force behind formation of the Association of Breast Surgeons of India, which is South Asia's first dedicated Breast Surgical Society and served as its founder honorary secretary (2011-2013) and president (2015-2017).

In appreciation of his outstanding academic track record, innovative initiatives that have transformed breast healthcare in India and life transforming personal philanthropy in his adopted village, the President of India conferred him with Padma Shri (2015), which is one of the highest civilian awards of the land, and Dr. B.C Roy National Award (2016), which is the highest recognition that can be achieved by a doctor practicing in India. He was recently recognised in Queen Elizabeth II's 2021 New Year's Honours list and achieved the rare distinction of becoming one of the youngest surgeons of Indian origin in over 100 years to be honoured by Her Majesty, The Queen with an OBE-Officer of the Most Excellent Order of the British Empire. This is the second highest ranking Order of the British Empire award (excluding a knighthood/Damehood) conferred in recognition of his services towards "improving breast cancer care and surgical education in India and to UK/ India relations".



With Professor Robert Mansel (right) at annual Conference of The Association of Breast Surgeons of India (ABSI) during the presidential term of Dr. Raghu Ram (left) (ABSICON 2017)

- Pillarisetti Raghu Ram, Querci Della Rovere: Oncoplastic Surgery for retro areolar breast cancer – a technical modification of the Grisotti Flap, Indian J Surgery, 2007;69: 160 – 162
- Thornton H, Pillarisetti Raghu Ram. 'Breast awareness' and 'breast self-examination' are not the same. What do these terms mean? Why are they confused? What can we do? Eur J Cancer. 2008; 44(15):2118-21
- Pillarisetti Raghu Ram, Querci Della Rovere. 'Oncoplastic Breast Surgery, Recent Advances in Surgery' edited by Prof. Irving Taylor & CD Johnson, Royal Society of Medicine Publication, London, 2009, Vol.32; Chapter 2, 11-26
- Pillarisetti Raghu Ram. Breast healthcare in India time for a paradigm change. Ann RColl Surg Engl (Suppl) 2011; 93:250–252
- Pillarisetti Raghu Ram, Guidubaldo Quercidella Rovere: Oncoplastic Breast Surgery. Indian J Surgery, 2012; 74(3): 255 -263
- 6. Pillarisetti Raghu Ram. Early detection of breast cancer -Finding an 'Indian solution to an Indian problem'. J Med Sci Res 2014;2(2):55-56.
- Radhakrishna S, Pillarisetti Raghu Ram. "Breast" (Chapter 53), Bailey & Love Companion guide, CRC Press (Taylor & Francis group), London, 2015; 448-464
- Somashekhar S. P, Agarwal Gaurav, Deo S. V. S, Chintamani, Pillarisetti Raghu Ram, Sarkar Diptendra, Parmar Vani. Indian Solutions for Indian Problems -Association of Breast Surgeons of India (ABSI) Practical Consensus Statement, Recommendations, and Guidelines for the Treatment of Breast Cancer in India. Indian J Surg, 2017; 79(4):275–285

- Pillarisetti Raghu Ram. "Perspective from India: Improving Breast Health Care" (Chapter 35) – "Breast Cancer: Global Quality Care" edited by Didier Verhoeven, Cary Kaufman, Robert Mansel, Sabine Siesling, Oxford University Press, 2020; 371-376
- Pillarisetti Raghu Ram. "2020—the Year That Was!". Indian J Surg, 2020; 82, 991–998



Dayalan Clarke, MS, FRCS (Edin) MD (Cardiff) FRCS (Gen), Consultant Breast, Oncoplastic and Breast Reconstructive Surgeon. Mr Clarke had his undergraduate medical training and post-graduate training in general surgery in Christian Medical College, Vellore, India. He moved to the UK in the early 1990s, and his first job in surgery in the UK was at the Cardiff Breast Unit. After his initial years of surgical training in South Wales, he returned to the Cardiff Breast Unit as a research fellow to work with Professor Robert Mansel and Professor Helen Sweetland. As a research fellow at the Cardiff Breast Unit, Mr. Clarke was responsible for setting up and running the ALMANAC trial-a randomised, multi-centre, two-phase, national trial in the UK that validated the routine use of sentinel node biopsy as the standard procedure to stage the axilla in breast cancer. This trial was funded by the Medical Research Council with Professor Robert Mansel as the Principal Investigator. Following the successful validation of a pilot study, he was responsible for putting together the trial protocol and the case report forms for the ALMANAC trial. The learning curve for sentinel node biopsy that was demonstrated in the ALMANAC trial resulted in the introduction of the NEW START training programme in the UK, which was responsible for training all breast surgeons in the country prior to the safe introduction of this surgical procedure for staging the axilla in breast cancer. He accomplished a dissertation on the performance of sentinel node biopsy based on the ALMANAC trial and was awarded an MD from the Cardiff University. Mr Clarke completed his training in breast surgery with an oncoplastic fellowship in Birmingham. He was appointed as a Consultant Breast, Oncoplastic and Breast Reconstructive Surgeon at the South Warwickshire NHS Foundation Trust in Warwick, UK. He was responsible for setting up a leading breast unit at Warwick. The Warwick Breast Unit was one of the early breast units to introduce "OSNA"-One Step Nucleic acid Assay-for the intraoperative assessment of the sentinel node. OSNA is a polymerase chain reaction (PCR)-based assay that detects the presence of Cytokeratin 19 in the sentinel node, and the result is available in 30-45 min, which allows for an immediate axillary node clearance at the primary operation. In Warwick, the sentinel node biopsy is performed as the first part of the operation, and while the sentinel node is being assessed by OSNA, the wide local excision or mastectomy is carried out. By the time the surgery on the breast is completed, the results of the OSNA are available, thus allowing one to proceed to an axillary node clearance for those patients whose sentinel node is positive on OSNA at the same operative procedure. After 15 years of working as a Consultant in Warwick, Mr. Clarke has taken an early retirement from the NHS with the intention of doing voluntary work in areas of need. He has recently concluded two, 6-month periods working in rural India.

- Sentinel Node Biopsy Edited by Hiram Cody (Chapter for textbook) Publishers – Martin Dunitz Ltd 2002 D. Clarke, R. E. Mansel. How we do it: The Cardiff University approach – Pages 237-44
- Sentinel Node biopsy in Breast Cancer: Results of a randomised multicentre trial - ALMANAC Trial - R Mansel, R Newcombe, L Fallowfield, D Clarke et al Journal Of National Cancer Institute Vol 98, No 9, May 2006 Pages 599-609
- Results of a national training programme in sentinel lymph node biopsy for breast cancer. RE Mansel, F Macneil, K Horgan, A Goyal, A Britten, J Townson, D Clarke et al. British Journal of Surgery. Vol 100, Issue 5, Pages 654-661, April 2013
- 4. The learning curve in sentinel node biopsy: The ALMANAC Experience D Clarke, R Newcombe, R Mansel. Annals of Surgical Oncology Vol 11, No 3, 2004
- 5. Injection techniques. D Clarke. A chapter for an e-book produced by the Raven Department of Education, Royal

College of Surgeons, England for the NEW START training programme.

- Intraoperative assessment of the sentinel node in breast cancer reduces time to commencement of adjuvant chemotherapy. N Rizkalla, K McEvoy, L Jones, S Harries, D Clarke. European Journal of Surgical Oncology, Vol 39,Issue 5,May 2013
- Do molecular assays for assessing the sentinel node result in upstaging breast cancer? A Zolnourian, S Harries, L Jones, D Clarke. European Journal of Surgical Oncology, Vol 39,Issue 5,May 2013
- Implementation of One Step Nucleic acid Amplification (OSNA) for the intraoperative assessment of sentinel nodes in a district general hospital. J Mecci, M Iqbal, S Harries, L Jones, D Clarke. European Journal of Surgical Oncology, Vol 38, Issue 5, May 2012
- Selective omission of blue dye in sentinel lymph node biopsy. Iqbal M, Waters J, L Jones, S Harries, D Clarke San Antonio Breast Cancer Symposium 2011 (AACR Journal)
- Is single node metastasis more common in sentinel node era? G Shetty, Iqbal M, S Randhawa, F Sandhu, J Simon, N Chachlani, L Jones, S Harries, D Clarke San Antonio Breast Cancer Symposium 2011 (AACR Journal)

Maureene Roberts worked extensively on breast disease and made some epoch making publications on breast screening with Prof APM Forest and moved with him to Edinburgh. John Forbes was a registrar, with Professor LE Hughes, who took up the speciality of breast disease. He became Professor of Oncology at the University of Newcastle, NSW, Australia. He was a major influence on breast cancer research in the Antipodes. **Roger Blamey** was an SHO in Cardiff and became professor of surgery at Nottingham and took on treatment and research in breast disease. Helen Sweetland was a consultant on the unit who also worked for several years on breast disease.

Many other trainees from India, namely, Drs. BS Srinath now practising surgical oncologist at Bengaluru; Arvidan Nair, Professor of Endocrine Surgery at CM Vellore; and VK Shukla and AK Khanna both Professors in Surgery at Institute of Medical Sciences Banaras Hindu University, had their post-doc training at Cardiff.

Declarations

Conflict of Interest The author declares no competing interests.

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.