Nuclear Medicine in Nottingham: Antibodies, Gamma Probes and Drug Delivery

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When I started work in Nottingham in 1980 University Hospital had only recently been built. The University of Nottingham Medical School and Hospital was officially opened by the Queen on 28 July 1977 and named 'Queen's Medical Centre'. At the time it was completed it was to be one of the biggest hospitals in Europe with over 1300 beds and 27 miles of corridor. The nuclear medicine department was equipped with a Siemens single head camera and was the first out patient department in the hospital to receive patients. This was one of three hospitals in Nottingham where nuclear medicine was undertaken, the other two being Nottingham City Hospital and the Nottingham General Hospital near Standard Hill, (named after the point where King Charles raised his Royal Standard in 1642, thus starting the English Civil War). In the early 1980s the General Hospital was still carrying out nuclear medicine scans on a rather old rectilinear scanner. When this facility was closed nuclear medicine was further developed at both Queen's Medical Centre and the Nottingham City Hospital. With the Medical School still being in its infancy there were many young clinical and scientific staff eager to make an impact and many diverse areas of research developed that involved nuclear medicine techniques.

The Cancer Research Laboratories at Nottingham University were a collection of old single story huts on the university site now occupied by the Biomedical Sciences Building, on the opposite side of the ring road to the Medical School. In the early 1980s Professor Robert Baldwin lead a team of 50 scientists who were developing the then new monoclonal antibody technology. Along with the University of Birmingham, and the Charring Cross Hospital, London, Nottingham pioneered the

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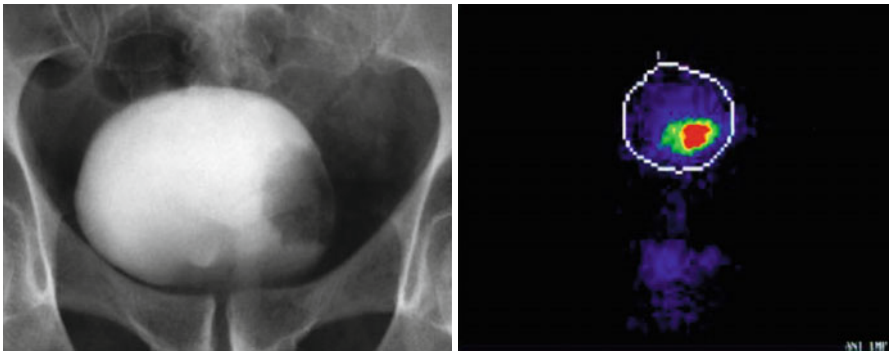

Fig. 13.1 An intravenous urogram and ^{67}Cu-C595 image in a patient with a superficial cancer of the bladder

in vivo use of monoclonal antibody imaging. One of the first antibodies to be used was 791t/36 produced from a patient with osteogenic sarcoma. The first clinical use of this antibody was carried out in patients with colorectal cancer [1]. The imaging was technically demanding since the first antibodies were radiolabelled with I-131 and the long survival of the antibody in the circulation necessitated the use of background subtraction employing Tc-99m-labelled human serum albumin [2]. The work with monoclonal antibodies progressed with Nottingham undertaking some of the first in vivo studies using In-111 and Tc-99m-labelled antibodies [3, 4] and published one of the first studies of SPECT antibody imaging [5]. Work with antibody fragments (Fab and F(ab')2) progressed and over the next 10 years the affects of antibody responses were observed leading to a decline in routine use. Therapeutic trials of Cu-67-C595 anti-MUC1 antibody in bladder cancer continued and this approach still offers unexplored potential Fig. 13.1 [6]. The European directives on the GMP conditions required for the production of biologicals including antibodies, meant that the Nottingham production facilities were no longer suitable for the manufacture of clinical grade materials and so the "home grown" antibody studies came to an end.

Other work in Nottingham led the way for the early use of intraoperative probes for the detection of lesions removed during surgery. Work started by John Hardy with one of the orthopaedic surgeons, Chris Colton in Nottingham led to the use of the gamma probe for the localization of osteoid osteoma Fig. 13.2 [7].

This pre-dated the use of gamma probes for sentinel node detection and led to the development of the RMD gamma probe in the United States. Over a period of 10 years I personally travelled from Southampton to Aberdeen assisting surgeons localize a variety of lesions [7, 8]. Similar techniques were developed for the use of probes in the intensive care unit [9].

Over the past 30 years Nottingham has been associated with other areas of nuclear medicine research. Working with Malcolm Frier a range of novel radiopharmaceutical products were developed and investigated including recombinant human

Fig. 13.2 The author using an early gamma probe in the operating theatre in the 1980s

serum albumin [10] a spin off from the Bass brewing industry and recombinant branched-chain polypeptide synthetics [11] and aptamers [12]. Perhaps more unique to Nottingham was the use of nuclear medicine techniques in the study of conventional drug delivery and formulation. Extensive studies were undertaken to image the release, delivery and biodistribution of formulations including enteric coated oral dose forms, enemas, eye drops, nasal sprays and aerosols [13–15]. Much of this work has involved the study of tablet swallowing [16], gastrointestinal transit, the understanding of gastrointestinal physiology and the development of nuclear medicine imaging techniques for the study of the gastrointestinal tract Fig. 13.3 [17].

These areas of work have continued with the application of magnetic resonance imaging in the study of gastrointestinal transit [18, 19].

More recently through a collaboration with John Lees at the Space Research Centre at Leicester University, Nottingham has been pioneering the first clinical use of a hand-held hybrid optical gamma camera for small parts imaging and for use in intraoperative imaging Fig. 13.4 [20]. Studies are continuing in collaboration with surgeons in Nottingham and Derby.

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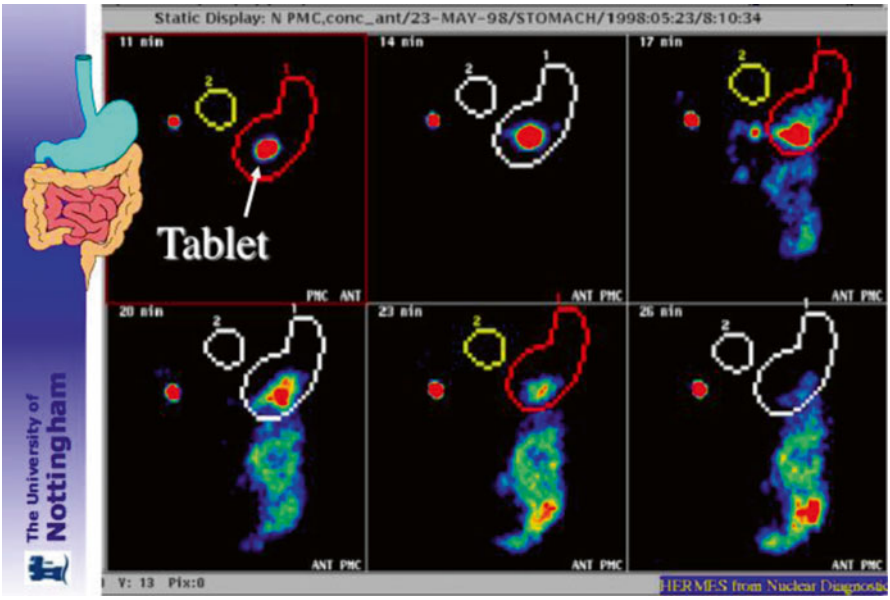

Fig. 13.3 Shows the process of a tablet in the stomach disintegrating and emptying into the small bowel

Fig. 13.4 A hand held intraoperative hybrid optical gamma camera

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