

**STFC Global Challenge Exploratory Award Report****Advances in Intraoperative Nuclear Imaging****John Lees, Alan Perkins and Sarah Bugby****Introduction**

We report on the one day meeting held in Leicester to explore how new technologies can be used to improve outcomes for cancer patients. The meeting, Advances in Intraoperative Nuclear Imaging, was held in College Court, Leicester, on the 17<sup>th</sup> February 2015. The event was by invitation only to ensure a strong focus on the meeting aims. A number of invited speakers from both the UK and Europe were invited to bring together experts in the emerging technologies and clinicians who will use and drive the development of new systems. In total there were 30 attendees from 21 different institutions along with 4 representatives from industry.

The original target audience were surgeons, clinicians, cancer researchers, clinical scientists/technologists (Medical Physicists and operating theatre staff) and technologists. This planned diversity was reflected in the attendees at the meeting.

Overall the meeting aimed to review and highlight recent developments of compact small field of view camera systems which offer significant potential for extending the role of nuclear medicine applications in surgical procedures. Areas covered included:

- SFOV camera systems, detectors and operation
- Hybrid gamma camera systems
- Hybrid tracers
- Clinical applications
- Surgical evaluation and user experience

**The full programme is attached as an appendix.**

**Meeting summary**

With the exception of a number of speakers (see below), attendees were from the UK with expertise in nuclear medicine, imaging and physics.

The speakers and a short synopsis of their presentations including a number of highlighted issues are now summarised:

Prof Alan Perkins, School of Medicine, University of Nottingham

**An overview of SFOV cameras and intraoperative applications**

Prof Perkins opened the meeting with a brief history of SFOV systems and intraoperative imaging, a description of the technologies currently available and in development and a list of current and potential future applications.

Dr Dimitra Darambara, Royal Marsden NHS Foundation Trust

#### **Detector design for SFOV Nuclear Cameras**

This presentation began with a review of the technical pros and cons of various detectors (scintillators, crystals/solid state, collimators, PMTs, CCDs, etc). Particular problems that are not addressed with current technology are the detection of small, deep-seated nodes and the differentiation of features in a non-uniform background. The identified 'needs' for an intraoperative imager were low cost, portable, improved sensitivity and spatial resolution and good image quality (related). High sensitivity is particularly important for tumour removal procedures: spatial resolution is more important for SLN procedures and if background noise dominates then a good energy resolution is required. In addition, it is important to be able to image all/most of the surgical FOV in a single image. Dr. Dimitra also introduced several methods of computational optimisation in developing new devices (such as finite element analysis, MC simulations, SPICE modelling and 4D mouse simulations).

Dr Marie-Alix Duval, IMNC, Orsay,

#### **Surgical experience with POCI and TReCam**

The design of and initial clinical experience with the first generation Per-Operative Compact Imager (POCI) and follow-up TreCam compact gamma cameras were presented.

These cameras have been used in a number of imaging studies related to breast cancer and the identification of lymph nodes. Limitations found during the study were that the camera head could not get close to the target and low sensitivity of the camera system. However, a study with the POCI indicated that an intraoperative camera was able to find nodes that non-imaging probes could not, that surgeons were satisfied with non-smoothed images, and that, except in complex cases, pre-operative imaging was deemed unnecessary. Results of the initial evaluation of TReCam have been accepted for publication in the *Quarterly Journal of Nuclear Medicine and Molecular Imaging*.

Other limitations of this technology were its weight (2.2 kg) as it is purely hand-held (no supporting arm) and that it is difficult to hold due to its angular design. It also uses a LaBr<sub>3</sub> crystal which, although having excellent technical characteristics, is extremely expensive to produce. Localisation with the TreCam involves centring activity on the screen, placing the camera directly onto the patient, and then drawing around it – not the most elegant solution but simple, quick and robust.

Dr Thomas Wendler, SurgicEye GmbH, Germany

#### **Intraoperative imaging with tracked detectors in the example of freehand SPECT and its hybrid extensions**

Dr Wendler gave a presentation (including video) on the use of the declipseSPECT, "free-hand SPECT", system. A video showing use of the system with a gamma probe can be found at: <http://www.surgiceye.com/en/declipseSPECT/openSurgery.html>. Hybrid images are 2D optical with 3D SPECT superimposed. A new 'Sentiguide' system combining ultrasound and SPECT is in development, with the aim of using

needle biopsy in SLN – this is in trials at the moment and some problems with image registration and depth differentiation were touched upon.

Mr. KL Cheung, Royal Derby Hospital Centre, University of Nottingham

#### **Clinical requirements and expectations – using sentinel node biopsy as an example**

Mr Cheung focused on breast and routine (NICE supported) clinical practice in the UK. He described the development of SLNB, highlighting the results of the ALMANAC trial and the START training programme. He confirmed that pre-operative lymphoscintigraphy with a LFOV camera was no longer performed in the UK as surgeons believe it to provide no value. He also emphasised that it would be impossible for any new technology to prove that it improved detection rates or reduced the false negative rate as that would require nodal clearance and biopsy which is no longer carried out in the UK.

With regard to unmet needs, the value of SLNB in patients having undergone neoadjuvant therapy was reviewed as was the hope to be able to dispense with the use of blue dye which can (infrequently) cause anaphylaxis and often unsightly tattooing of the skin.

Gamma probes (some of which are now wireless) are at the heart of the SLNB procedure and it seems highly likely that any imaging technique will be regarded as an addition to use of the gamma probe rather than as a replacement to it. This certainly has implications for overall cost-effectiveness.

Dr Bas Pouw, NKI, Amsterdam

#### **Surgical experience with intraoperative cameras**

Dr Pouw give a very detailed presentation on breast SLNB procedures at Netherlands Cancer Institute (NKI).

NKI performs 600 breast procedures/annum with 25-30% (and growing) in non-palpable cancers due to the success of screening procedures. Approx. 40% of cases will have received neoadjuvant therapy prior to surgery.

Unlike in the UK, pre-operative lymphoscintigraphy with a LFOV camera is performed 15 mins and 3 hours post-injection of  $^{99m}\text{Tc}$ -nanocoll to evaluate drainage patterns and identify sentinel nodes and higher echelon nodes (i.e. nodes downstream of the sentinel nodes). NKI also implant a decayed  $^{125}\text{I}$  (~8MBq activity) seed (used for treatment of prostate cancer) into the tumour to aid localisation in the operating room. They routinely perform a 2-day protocol which allows Tc decay aiding discrimination between the  $^{99m}\text{Tc}$  and  $^{125}\text{I}$  energies (140 and 35 keV) in the operating room. For these procedures standard probes are usually the best technique, in some cases where depth information is important Freehand SPECT is used.

Prof. Mark McGurk, King's College, London

#### **Radio-Guided Surgery in Oral Cancers – Hybrid Imaging and Hybrid Tracers**

Prof. McGurk gave a presentation on the challenges involved in the surgery of oral cancers and emphasised the potential of fluorescent tracers (see Ms van den Berg's presentation below). The main causes of higher false negative rates for SLNB (13%) are inadequate static imaging, no dye used, inexperienced personnel and unusual locations (i.e. tumours unexpectedly mapping to nodes on the other side of the

neck). He suggested that Freehand SPECT takes around 10 minutes to detect nodes based on 10-80MBq Tc. Freehand SPECT gives a 93% positive detection rate, comparatively SPECT-CT has 100%. Integration times for fluorescence images are typically 10 – 20 seconds.

Ms Nynke S. van den Berg, Leiden University Medical Center

#### **New intraoperative techniques for sentinel node detection in the head and neck area**

This presentation indicated that SPECT-CT is the preferred pre-operative imaging modality due to the variable drainage patterns of head and neck tumours, the large numbers of nodes and the concentration of blood vessels and nerves. However, patient position during SPECT-CT is not the same as patient position during surgery and this may cause some difficulties. The tools typically used during theatre for SLNB at Leiden are as follows;

1. Sentinella: 2D overview image
2. CrystalCam/Declipse: GoPro videos showed surgeon looking back and forth from patient to screen. There is more scatter than in pre-surgery images so this is not ideal.
3. Freehand SPECT: Switched to as gives depth information along with an acoustic output.
4. Fluorescent (Photodynamic Eye): Operating lights must be dimmed as they emit NIR, fluorescence images are taken then lights turn back on (for very bright nodes the lights can remain on). Nodes are then imaged after excision.
5. Sentinella: Reimage of the whole operating area to check nodes have been removed.

Focus on the use of fluorescent tracers and particularly hybrid tracers ( $^{99m}\text{Tc}$ -Fluorescent marker). Leiden are producing their own  $^{99m}\text{Tc}$ -Nanocoll coupled to indocyanin green but mentioned that GE Healthcare are also beginning to supply this hybrid tracer to a number of sites in Europe.

In addition to imaging with a fluorescent camera, the group are also using the “OptuNuclear” probe which is a conventional gamma probe modified to detect a fluorescent signal and provide an audible alert with the volume dependent on the strength of the signal. As fluorescence is only used for confirmation currently there is no real preference between a probe and a camera.

Dr John Lees, University of Leicester,

#### **Hybrid gamma-optical imaging**

Dr Lees gave a presentation on hybrid optical and gamma imaging. Images from the clinical environment were presented showing the gamma activity overlaid onto an optical image of the patient. Attendees were particularly impressed with the optical capability and resolution of the system.

## Meeting Summary and Outcomes

Overall the meeting was viewed as highly educational and extremely useful for building relationships between clinical investigators, STFC researchers and end-users. To summarise the discussed topics;

- Fluorescent tracers, and in particular hybrid nuclear-fluorescent tracers, are likely to be developed and be adopted in the clinic. A literature search for details of agents in development should be a priority.
- 3D imaging is certainly preferred to planar imaging.
- There was no mention of cost-effectiveness in any of the presentations. Developments of health-economic evidence to support new camera developments were seen as a key differentiating factor, particularly in the US.
- The number of procedures in patients with non-palpable tumours and the number of patients receiving neoadjuvant therapy has increased significantly over recent years and this trend seems likely to continue. The implications of these factors for routine clinical practice of SLNB and clinical development programme needs to be discussed in detail with Key Opinion Leaders.

## Outcomes

- Two follow-on workshops are planned for the Summer and Autumn 2015 to focus on developing an internal network on healthcare expertise and on industrial engagement
- Aim to develop a more formal Network. STFC have an upcoming call which may support this.
- Collaboration between Universities of Leicester and Nottingham with Leiden University Medical Center and NKI, Amsterdam
- Prior to the meeting we were approached by the publisher CRC Press Taylor & Francis to consider a book reflecting the topic of the meeting. It was decided that each of the invited speakers would contribute a chapter to the proposed text book. The aim is to publish early in 2016.

## Advances in Intraoperative Nuclear Imaging

A one day meeting on the use of interventional nuclear imaging

College Court, University of Leicester 17 February 2015 10am – 16.30

### FINAL PROGRAMME

9.30	<i>Coffee and registration</i>
10.00	Prof Alan Perkins, School of Medicine, University of Nottingham <b>An overview of SFOV cameras and Intraoperative Applications</b>
10:35	Dr Dimitra Darambara, Royal Marsden NHS Foundation Trust <b>Detector design for SFOV Nuclear Cameras</b>
11:10	Dr Marie-Alix Duval, IMNC, Orsay, <b>Surgical experience with POI and TRCam</b>
11:45	Dr Thomas Wendler, SurgicEye GmbH, Germany <b>Intraoperative imaging with tracked detectors in the example of freehand SPECT and its hybrid extensions</b>
12:20	Discussion
12:30	Lunch
13:30	KL Cheung, Royal Derby Hospital Centre, University of Nottingham, <b>Clinical requirements and expectations – using sentinel node biopsy as an example'</b>
13:40	Dr Bas Pouw, NKI, Amsterdam <b>Surgical experience with intraoperative cameras</b>
14:15	Prof Mark McGurk, Kings College London <b>Radioguided Surgery in Oral cancers-Hybrid imaging and Hybrid tracers</b>
14:50	<i>Tea/coffee</i>
15:00	Dr Nynke S. van den Berg, Leiden University Medical Center, <b>New intraoperative techniques for sentinel node detection in the head and neck area</b>
15:35	Dr John Lees, University of Leicester, <b>Hybrid gamma-optical imaging</b>
16:10	Discussion
16:30	Coffee + Networking

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