

NAVIGATED NUCLEAR PROBES FOR INTRA-OPERATIVE FUNCTIONAL IMAGING

Nassir Navab, Joerg Traub, Thomas Wendler

Computer Aided Medical Procedures
(CAMP), TUM, Munich

Andreas Buck, Sibylle I. Ziegler

Department of Nuclear Medicine,
Klinikum rechts der Isar, TUM, Munich

ABSTRACT

Since the 1920s, functional imaging has continuously contributed with novel methods in medical diagnostics. Its usage in the operation room has been limited in the past, although there is a great potential for localization of target structures and control of the surgery outcome. One example of functional information in the operation room is the use of nuclear probes. These devices are radiation detectors that provide a 1D signal that allows the surgeons to get information about the distribution of a radioactive labeled structure. We extended nuclear probes with a spatial localization system in order to generate functional 3D surface images or functional tomographic images in the operating room. In this paper we summarize our methodology, discuss current limitations and possible remedies, and provide an outlook towards a new generation of image guided surgery based on anatomical and functional intraoperative imaging.

Index Terms— Biomedical nuclear imaging, Image reconstruction, Beta-ray detectors, Gamma-ray detectors, Surgery

1. FUNCTIONAL IMAGING IN THE OPERATING ROOM

In surgery, the radically different type of information of nuclear medicine has made it to an important and complementary source of information for surgical planing. All around the world for example F-18-FDG PET is used to distinguish malignant abnormal structures (tumors, metastasis infected lymph nodes, etc.) from benign ones, playing a crucial role in the management of therapy and planing of the operation [1].

In the operating room itself, the preoperatively acquired images are commonly available, but unfortunately they are only used for approximate guidance due to patient movement, organ deformation, changes in the functional properties of the tissues or partial resection during the surgery.

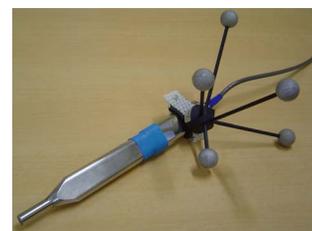
Due to these limitations and to the motivation of extending the success of nuclear medicine in the field of diagnostics, efforts have been made to obtain nuclear medicine images directly in the operating room.

The history of intra-operative nuclear medicine starts in the 1960s with the introduction of hand-held nuclear probes.

A nuclear probe is a one-dimensional hand-held measurement device that consists of a single detector with a proper collimation (cf. figure 1). This device can be used in the operating room and allows free movement for finding sources of radiation in the body [2].



140 keV and 511 keV
gamma probes.



beta probe with an
optical tracking target.

Fig. 1. Nuclear probes by IntraMedical imaging, Los Angeles, CA, USA.

The use of a gamma-detecting probe (short gamma probe) led to the introduction of the so-called radio-guided surgery, which has become a standard in breast cancer [3] and melanoma [4].

Due to the statistical nature of the radiation readings, they only give an indication of the location of the radiation sources in presence of a low signal-to-background rate. They further suffer from the potential danger of missing a source as they rely on a thorough scanning of the region of interest. Further pitfalls are the effects of "shadowing" and "shine-through" which increase the false-negative rates [5].

In order to overcome these limitations, so-called mini-gamma-cameras were introduced (e.g. [6]). These devices are essentially arrays of gamma probes that allow the generation of small field of view 2D images. However, the increased amount of information enabled by bigger and heavier systems reduces their flexibility.

The growing demand for flexible, confident, and precise functional imaging for minimally invasive surgery encourages the development of alternative solutions to enable comparable nuclear imaging quality in the operating room.

2. FUNCTIONAL IMAGING WITH NAVIGATED NUCLEAR PROBES

To take advantages of nuclear probes and to generate intra-operative functional images, our group introduced the idea of combining currently available probe systems with position and orientation tracking systems [7, 8].

The basic idea is to scan the region of interest with a tracked probe, while simultaneously collecting the measurements of the radiation detector and its position and orientation. Based on the collected data new images can be reconstructed depending on the type of radiation. In case of beta-radiation, a 3D radiation surface distribution and in case of gamma-radiation a 3D tomographic radioactivity distribution (cf. figure 2) are reconstructed.

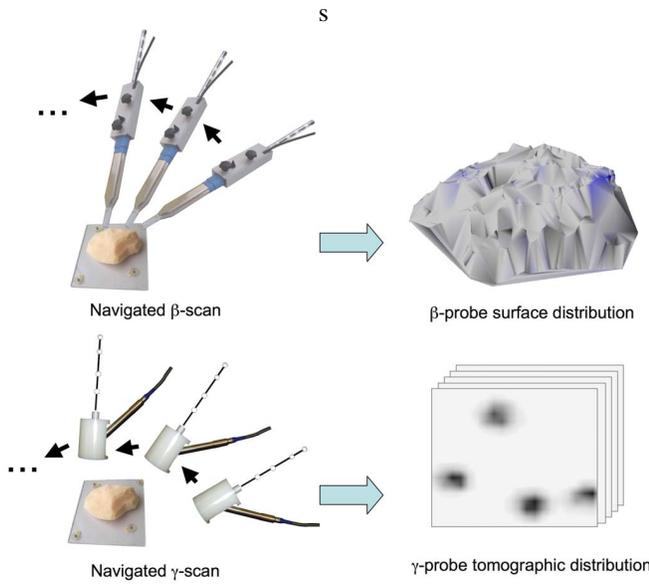


Fig. 2. Idea of reconstructing radioactivity distributions from a tracked nuclear probe. Above a tracked beta probe allows the reconstruction of a 3D surface distribution. Below from a tracked gamma probe scan a 3D tomographic image is generated.

The traditional reconstruction problem of nuclear medicine imaging has to be thus restated. Using the standard linear assumption, the problem can be stated as:

$$g_i = \sum_j h_{ij} f_j, \quad (1)$$

where g_i is the reading of the tracked nuclear probe at time i and f_j is the activity concentration to be reconstructed at a certain position j on top of the surface for beta probes or in the tomographic volume for gamma probes. The coefficient h_{ij} (entries of a so called system matrix) describes the influence of a unitary radiation source at position j to the count rate at time i .

In contrast to the traditional approach in nuclear medicine, the determination of these coefficients cannot be made a priori, as the relative positions and orientations of the sensor to the source is not fixed and depends on the scan. The coefficients h_{ij} thus need to be calculated during runtime.

To determine the coefficients of the system matrix, a forward model of the acquisition process is used. In that case we would have:

$$h_{ij} = F(\vec{x}_i, \vec{x}_j, \vec{t}, \vec{d}), \quad (2)$$

where F is a non-linear function of the position of the sensor \vec{x}_i , the radiation source \vec{x}_j and the parameters of the tissue in between \vec{t} , as well as the ones of the detector \vec{d} . Due to the requirements on calculation time only the use of simple fitted analytical models or look-up tables are reasonable alternatives [9].

In any case two calibration steps are required:

1. the determination of the transformation from the coordinate system of the tracking sensor to the radiation sensor (cf. figure 2),
2. the determination of the parameters of the model to be used to calculate the coefficients of the system matrix.

As most probes have cylindrical sensors, the first calibration step can be accomplished using an auxiliary calibration target. This auxiliary tool fits the sensor per construction and has a tracking target attached (cf. figure 2). By rotating it around the sensor and acquiring the relative position, the axis of the sensor and the front face can be calculated.

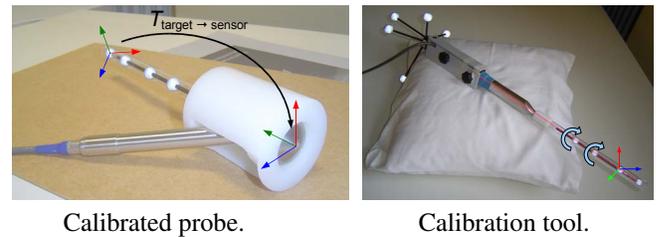


Fig. 3. First step of calibration for tracked probe with cylindrical sensor.

In the second step the radiation acquired by the sensor is measured at different relative positions from a known source. Our protocol includes the use of a 2D linear positioning robot. This robot is controlled automatically to move the source of radioactivity in a plane. The probe is held during the process in a fixed position. The distance to the plane can be moved in known steps. The outcome of this acquisition procedure is a set of statistically valid radiation values associated to a regular grid of spatial positions. This set of readings can be used to calculate the required parameters (e.g. the vectors \vec{t} and \vec{d}) of the model.

The next step is to reconstruct the surface or tomographic volume from the readings. We have chosen to use the iterative reconstruction approach used in conventional nuclear medicine imaging [10]. The analytic approach is unfortunately not possible here as it needs a set of projections which is complete and dense.

As a summary, the complete process of off-line and on-line calculations can be stated as following:

1. Off-line step
 - (a) Determination of transformation between sensor and tracking target of probe.
 - (b) Determination of parameters of model to be used for reconstruction.
2. On-line step
 - (a) Definition of volume or surface to be reconstructed (it can be eventually done during data acquisition if the movement of the probe is used).
 - (b) Simultaneous acquisition of probe read-out, position and orientation.
 - (c) Calculation of h_{ij} for every reading i and position j at which radioactivity is to be reconstructed using the model.
 - (d) Reconstruction of the radioactivity distribution inverting system matrix.

3. INTO THE OPERATING ROOM

In our preliminary work, the methodology presented in the previous section was shown to be feasible and capable of generating promising images of both surfaces and tomographic volumes (cf. figure 4). There is still much work to be done before going to the operating room.

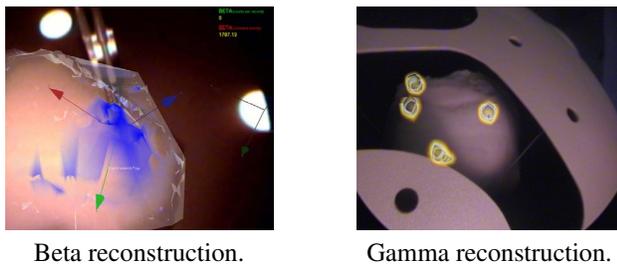


Fig. 4. Left: Radioactivity surface reconstruction using a tracked beta probe [7]. Areas in blue present a higher uptake than area in white. Right: [8].

The first issue to be considered is that the reconstruction algorithms do not compensate for the fact that the set of readings is neither dense nor complete. In that sense, due to the ill-posed nature of the reconstruction problem, invalid images can be reconstructed.

To compensate for this, we monitor the quality of the acquisition in terms of the validity of the reconstruction they generate. This can be done for example by looking at the condition number of the system matrix. We are currently developing automatic ways to determine a minimum threshold for the condition number of the system matrix in order to guarantee a valid reconstruction.

Our experiments have shown that a good method to acquire a dense set of projections is to show the scanned positions. This enables an approximate homogeneous distribution.

A second issue is that we implicitly assume that the surface or volume where the radioactivity distribution is to be reconstructed does not move, nor deform during the 1 – 2 min acquisition. We are currently working on strategies to avoid motion artifacts by detecting deformation and movements and by making the surgeon aware of the limitations. Possible solutions are to track the position of different features in the operation situs, track the anatomy using surface acquisition devices or combine the system with real-time anatomical images like ultrasound (e.g. as done in [11]) to detect potential sources of motion artifacts.

It is important to mention that the generated images are not meant to be real time images, but to be snapshots of the current functional state in order to decide on the immediate next steps in the surgery. Detecting the movement or deformation during a scan and eventually asking the surgeon to perform a new scan is then sufficient.

4. CLINICAL IMPACT

Throughout the paper a radically new technology for intra-operative functional imaging has been introduced. Its clinical impact has to be evaluated within the target applications.

For the beta probe surface reconstruction the primary clinical application is the definition of the resection borders of a cancerous tumor. Nowadays the resection borders of most tumors are defined by the surgeon in-situ trying to minimize the risk of local recurrence while keeping as much healthy tissue as possible. The only control of this decision is a fast analysis of 30 – 50 min called frozen section [12]. This technique is standard and provides some information on the completeness of the resection while the patient remains in the operating room. Based on the result of this frozen section the surgeon closes the patient or enlarges the resection borders. In the second case only vague information is available on the position of the detected cancer in the border regions. The marking of tumor cells with beta-emitting tracers like F-18-FDG, would allow a reliable scan of the tumor bed after resection and thus allow a localization of remaining malignancy and the possibility of minimizing the resection margins. Currently we focus in our hospital on the adaptation of the beta probe system for maxillofacial surgery. This application is of particular interest due to the complex anatomy and the impossibility of

cutting generously because of physiological reasons. Further, the technique of frozen section can be applied only with limitations to bony structures [12], which are usually involved in maxillofacial tumors.

For the 3D tomographic reconstruction the target application is 3D imaging for sentinel lymph node biopsy in breast cancer. Cancer usually expands over the lymphatic system. This makes a thorough investigation of the first lymph node downstream a useful diagnostic procedure to determine the probability of metastasis and thus to define the therapeutic steps ahead [5]. The localization of this first node (also known as sentinel lymph node or SLN) and its biopsy is a standard technique. There is however space for improvement. Complementing the preoperative imaging and the interventional use of gamma probes with intra-operative tomographic imaging, as presented here could enable a far less invasive surgery by reducing the inspection time. Furthermore the nature of the 3D imaging system could minimize major issues in the current approach like the shine-through and the shadowing effects. Among many other improvements, the major advantage may be the confidence that can be gained by acquiring a 3D image after the biopsy and thus confirming that the nodes resected were the sentinel ones. A prototype system for this application is currently being tested in our lab.

These two applications are just examples of a long list of surgical procedures where flexible, navigated functional imaging in the operating room would open new space for process optimization and intra-operative validation which could lead to overall improvement of the outcome.

5. CONCLUSIONS

In this paper we provide an overview of the emerging technologies allowing navigated nuclear probes to bring surface and tomographic functional imaging into the s. In conjunction with proper radioactive tracers, this technology may allow the surgeon to confidently resect cancerous tumors or any radioactively marked structure and intra-operatively verify the completeness of resection. This may open many opportunities for developing a new generation of surgical techniques taking full advantage of intra-operative functional and anatomical imaging.

6. REFERENCES

- [1] J. Gaa, H. Wieder, M. Schwaiger, and E. J. Rummeny, "Modern imaging for liver metastases from colorectal tumors," *Chirurg*, vol. 76, no. 6, pp. 525–6, 528–34, Jun 2005.
- [2] E. J. Hoffman, M. P. Tornai, M. Janecek, B. E. Patt, and J. S. Iwanczyk, "Intraoperative probes and imaging probes," *Eur J Nucl Med Mol Imaging*, vol. 26, no. 8, pp. 913–935, August 1999.
- [3] G. H. Lyman and et al., "American society of clinical oncology guideline recommendations for sentinel lymph node biopsy in early-stage breast cancer," *J Clin Oncol*, vol. 23, no. 30, pp. 7703–7720, Oct 2005.
- [4] J. Vaquerano, W. G. Kraybill, D. L. Driscoll, R. Cheney, and J. M. Kane, "American joint committee on cancer clinical stage as a selection criterion for sentinel lymph node biopsy in thin melanoma," *Ann Surg Oncol*, vol. 13, no. 2, pp. 198–204, 2006.
- [5] H. Rempp, *Sentinel lymph-node radiodetection in breast cancer: Results of a clinical study and development of a quantitative approach*, Ph.D. thesis, University de Nice Sophia-Antipolis, 2003.
- [6] J. M. Benlloch, M. Alcaniz, B. Escat, M. M. Fernandez, M. Gimenez, R. Gomez, V. Grau, C. Lerche, J. L. Palmero, N. Pavon, M. Rafecas, F. Sanchez, and D. Vera, "The gamma functional navigator," *IEEE Trans Nucl Sci*, vol. 51, no. 3, pp. 682–689, Jun 2004.
- [7] T. Wendler, J. Traub, S. I. Ziegler, and N. Navab, "Navigated three dimensional beta probe for optimal cancer resection," in *Proc. of MICCAI*. 2006, vol. 1 of *LNCS 4190*, pp. 561–569, Springer.
- [8] T. Wendler, A. Hartl, T. Lasser, J. Traub, F. Daghighian, S. I. Ziegler, and N. Navab, "Towards intra-operative 3d nuclear imaging: reconstruction of 3d radioactive distributions using tracked gamma probes," in *Proc. of MICCAI*. 2007, vol. 2 of *LNCS*, pp. 909–917, Springer.
- [9] A. Hartl, T. Wendler, T. Lasser, J. Traub, S. I. Ziegler, and N. Navab, "Towards intra-operative 3d nuclear imaging: development and evaluation of ad hoc models," in *Proc. of CURAC*. Deutschen Gesellschaft fr Computergesttzte Chirurgie, Oct. 2007.
- [10] M. N. Wernick and J. N. Aarsvold, *Emission Tomography: The Fundamentals of PET and SPECT*, Academic Press, 2004.
- [11] T. Wendler, M. Feuerstein, J. Traub, T. Lasser, J. Vogel, F. Daghighian, S. I. Ziegler, and N. Navab, "Real-time fusion of ultrasound and gamma probe for navigated localization of liver metastases," in *Proc. of MICCAI*. 2007, vol. 2 of *LNCS*, pp. 252–260, Springer.
- [12] M. M. Bui, P. Smith, S. V. Agresta, D. Cheong, and G. D. Letson, "Practical issues of intraoperative frozen section diagnosis of bone and soft tissue lesions," *Cancer Control*, vol. 15, no. 1, pp. 7–12, Jan 2008.