

# Tracking-based statistical correction for radio-guided cancer surgery

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**Abstract.** Radio-guided control of tumor resection borders can be provided by intra-operative hand-held beta-probes. As radioactive decay and its detection follow a statistical process the readings detected with such probes suffer from a high variance over time. In general their measurements are averaged over a certain duration, e.g. 1 – 3 [s], in order to provide statistically reliable measurements. This results in a smearing of the readings over an area if the probe is moved and thus in the risk that microscopic cancer residuals remain undetected.

To deal with this problem a statistical correction based on tracking of the hand-held detector is introduced. By extending the probe with a tracking system, statistical correction of the readings with a position-filtering approach is possible. In addition the new system allows calculating the confidence level of the estimated probe measurements in the region of interest, which is displayed interactively. This enables guiding the surgeon during the acquisition, making the process less user dependent and more robust.

The results do not only prove the concept, but show the superiority of the novel approach. A correlation with the ground truth of 53 – 75% versus 38 – 51% of the standard procedure was achieved. We show in this paper how computer assistance contributes to advanced visualization and guidance in surgery, as well as how it supports improving the quality of the acquired data.

## 1 Introduction

Lately intra-operative nuclear medicine guided procedures have been introduced in cancer surgery in order to allow radio-guided control of tumor resection borders. In this procedure, a radioactive tracer that accumulates primarily in tumors cells (i.e. FDG) is injected into the patient before the intervention. After the main tumor is resected with minimal resection margins, a hand-held radiation detector, i.e. a beta-probe, is used to find microscopic cancer residuals in the tumor bed, as these present higher count rates over the background radiation [1, 2]. This procedure allows the surgeon to selectively expand the resection borders.

The acquisition of radiation readings is a statistical process due to the random nature of the radioactive decay. In standard procedures this results in noisy or

even invalid data. Moreover it forces the use of temporal smoothing, like moving average filters with durations of 1 – 3 [s]. Unfortunately, the filtering introduces another pitfall for moving, hand-held probes: small radioactive ‘hot spots’ are smeared out and thus can vanish amidst the background radiation.

The combination of beta-probes with tracking systems was introduced for computer-assistance in cancer resection procedures for advanced visualization and instrument guidance [3]. By scanning the resection borders with synchronous recording of position, orientation and radio-active beta-probe measurements, they reconstructed surfaces showing an activity distribution.

To the authors’ knowledge, there exists no work that compensates for the statistical variance of the readings, which results in noisy and smeared surface measurements. In this paper we introduce new concepts for a computer-assisted intervention system by statistically correcting the readings of a tracked beta-probe using maximum likelyhood estimators and spatial information rather than filtering over time.

The statistical compensation is used to implement a computer-assisted guidance of the acquisition process, which results in a less user dependent and more robust procedure.

## 2 Materials and Methods

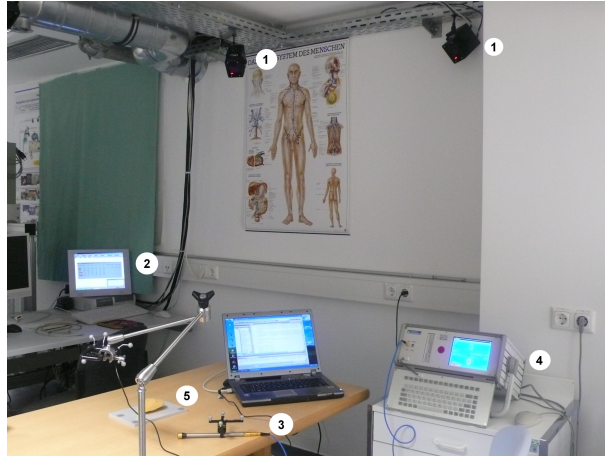
### 2.1 System setup

A hand-held beta-probe (Silicon Instruments GmbH, Berlin, Germany) was combined with an infrared optical tracking system in order to acquire the position and orientation of the probe synchronously with its readings (cf. figure 1). The tracking system consists of four ARTtrack2 infrared tracking cameras (Advanced Realtime Tracking GmbH, Weilheim, Germany). The cameras are located so that they are able to track a volume of  $2 \times 2 \times 2$  [m<sup>3</sup>] in which they achieve a root mean square (rms) error of 0.4 [mm] for the target position and 0.002 [rad] for the orientation according to the manufacturer’s specification (maxima 1.4 [mm] and 0.007 [rad], respectively).

### 2.2 Probe calibration

The calibration of the beta-probe consists of two steps. In a first step, the rigid transformation from the attached tracking target to the detector is determined. A linear 5DOF tracking target is used that is aligned with the axis of the probe. This is the distance between the tracking target and the detector along the axis of the probe.

In a second step, the field of view of the probe is obtained by acquiring the measurements of the beta-probe due to a single point source of radiation located at different, well defined positions. For the source, a cellulose scaffold of  $2 \times 2$  [mm<sup>2</sup>] with one ‘hot spot’ of <sup>18</sup>F-2-fluoro-2-deoxy-D-glucose (FDG, 1 [MBq/ml]) is placed on a 3-axes positioning table. The measurements of the



**Fig. 1.** The system setup consists of (1) tracking cameras, (2) tracking computer, (3) tracked beta-probe, (4) probe computer, and (5) radioactive phantom.

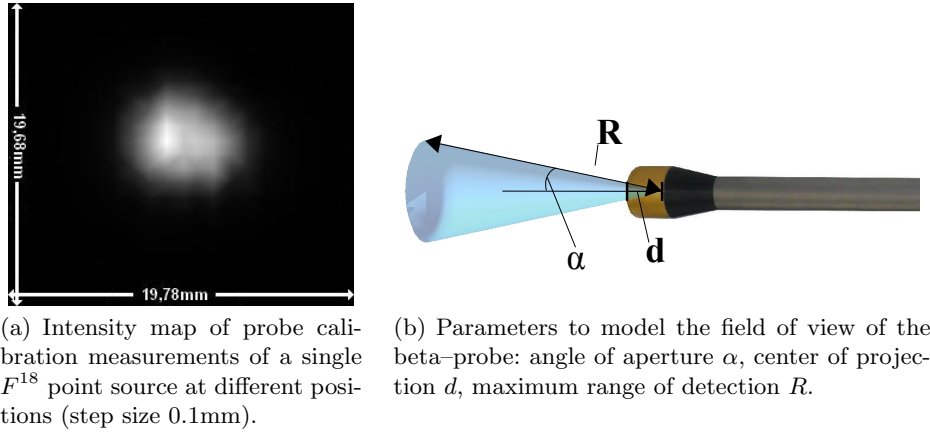
beta-probe at each distinct position with step size of  $0.1 [mm]$  are averaged over  $10 [s]$  to ensure a certain statistical reliability (fixed height of  $1 [mm]$  over source). The resulting uniformly spaced data-set (cf. figure 2(a)) is then analyzed to determine the parameters of the field of view of the beta-probe (cf. figure 2(b)).

### 2.3 Statistical correction and confidence calculation

For the position-based statistical correction and confidence calculation a 2D grid is interactively defined by the user on the region of interest. A surface reconstruction with a tracked infrared laser pointer is performed before that (as proposed in [4], mean quadratic error is  $1.8 \pm 0.4 [mm]$ ) to enable projection of the grid onto the phantom with correct height information.

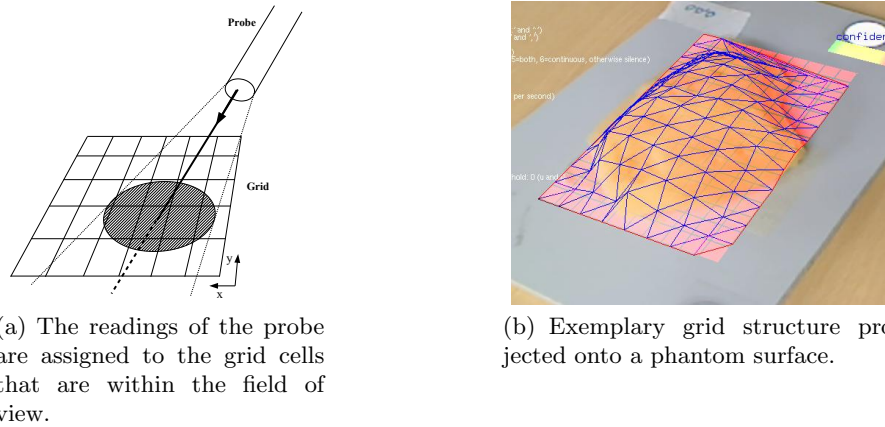
The relative position and orientation of the tip of the probe to the grid is used to calculate the contribution of each probe measurement to each distinct grid pixel (cf. figure 3(a)). This is achieved by defining a virtual camera with the same properties as the probe and then rendering the scene from the view of the probe. We use the center of projection, the field of view, and the maximum range of detection as the ‘far’ plane of a standard OpenGL camera within the rendering pipeline. The reading acquired and the contribution of each grid cell to the reading is then stored for further processing. The contribution to a certain grid position is defined as the probability that the current reading was originated solely because of the said grid position. An ad-hoc model of the acquisition process is required, see [5] for more details.

In order to correct for the statistics all contributions and probe readings for each grid position are given an optimal estimator. In case of a Poisson distribution, which is a standard model for both the decay and detection process of



**Fig. 2.** Experiment and model for beta-probe calibration.

radioactivity with high decay rates, the maximum likelihood estimator is the average of all readings. The confidence of the estimation at each grid point is also calculated using the readings obtained so far in an algorithm based on Pearson's  $\chi^2$ -goodness-of-fit test [5]. This value represents the probability that the measurements are related to a Poisson process with their mean measurement as expected value.

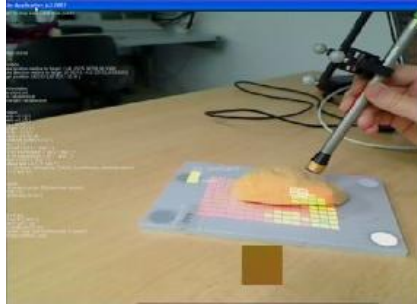


**Fig. 3.** A discrete grid is defined and mapped to the surface. The measurements of the probe at each distinct position contribute to several pixels within the grid.

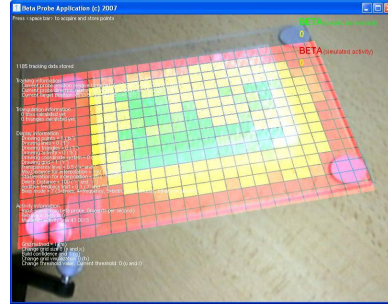
## 2.4 Computer-assisted acquisition

The availability of the confidence enables guidance of the scanning process. This solves the current problem of not being able to guarantee that the control of the resection borders was thorough enough and that no spot was not controlled for sufficient time to have a statistically valid reading.

In this work the guidance of the surgeon during the acquisition of the data was achieved by calculating the confidence at all grid points in real time and visualizing its value in every grid cell by means of augmented reality (figure 4(b)). The value was encoded with a color in the range from red to green, where green indicates a high level of confidence and red a low level of confidence. These results in an intuitive way to exhibit which areas require additional measurements.



(a) Guided beta-probe scan process.



(b) Incomplete beta-probe scan.

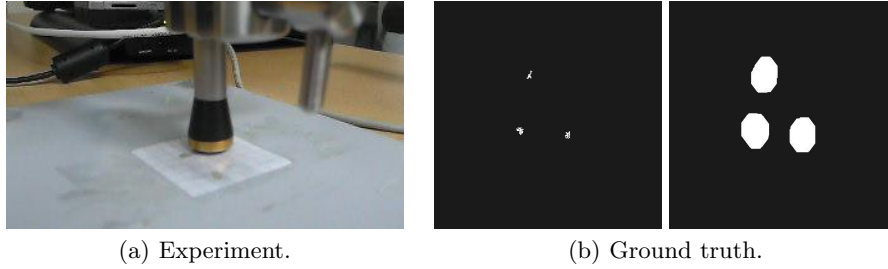
**Fig. 4.** Visualization of confidence values during the scan (a) and at the end of a scan procedure (b). Confidence values are overlaid onto an image of a video camera in real time. Green indicates cells with a high confidence level, red indicates a low confidence level and recommends an additional scan within these areas.

## 3 Experiments and results

For the experiments two flat cellulose phantoms with three ‘hot spots’ each ( $100 [kBq/ml]$ ) were used, one with a background radioactivity ( $10 [kBq/ml]$ ) and the other without background radiation. The confidence grid was fixed to the corners of the phantoms.

The ‘hot spots’ were colorized differently, enabling the ground truth to be obtained by scanning the phantom with an office scanner and segmenting them using a region-growing approach. The ground truth image was then registered to the grid using a 2D point-based registration (reprojection mean error  $0.03 [px]$ ).

Furthermore, the image of the ground truth was dilated by a morphological operator defined from the field of view of the probe. This was meant to simulate the fact that the probe is not a point measurement and that the sensitivity is almost constant in a radius of  $3.11 [mm]$  (figure 2(a)).



**Fig. 5.** (a) A cellulose phantom with three ‘hot spots’. (b) Segmented and dilated ‘hot spots’.

For both phantoms seven sets of measurements were obtained by different test persons. The visualization of the confidence was used in all cases. The number of measurements was  $1513 \pm 107$  for a duration of  $215 \pm 35$  [s]. The pixel size of the grid was set to be  $2.5$  [mm] for a  $3 \times 3$  [cm<sup>2</sup>] area.

For each set reconstructions of the surface radioactivity were performed using directly the raw data, a  $1$  [s] moving average time filter (equivalent to clinical standard procedure) and the position-based statistical correction. All three reconstructions were then compared with the ground truth.

In all reconstructions with and without background radiation the ‘hot spots’ could be clearly identified when statistical filtering was used (cf. figure 6). Furthermore the images generated were very smooth and did not present the noise patterns that were reported in the literature [3]. With the standard time filtering approach an identification of the ‘hot spots’ in the reconstructed image was difficult, in particular in presence of background activity.

For a quantitative comparison the normalized cross correlation (NCC) and normalized mutual information (NMI) between the reconstructed surfaces and the ground truth was computed. In all reconstructions the position-based statistical filtering was superior with both NCC and NMI.

## 4 Discussion

In this work the idea of using tracking and statistical models for the correction of beta-probe readings was introduced. The concept of computer-guided scanning was presented for the first time. The results show that such a computer-assistance can reduce the risk of missing microscopic cancer residuals in procedures like beta-probe control of resection borders. The use of this information for the reconstruction of radioactivity surfaces was proved to be statistically more robust.

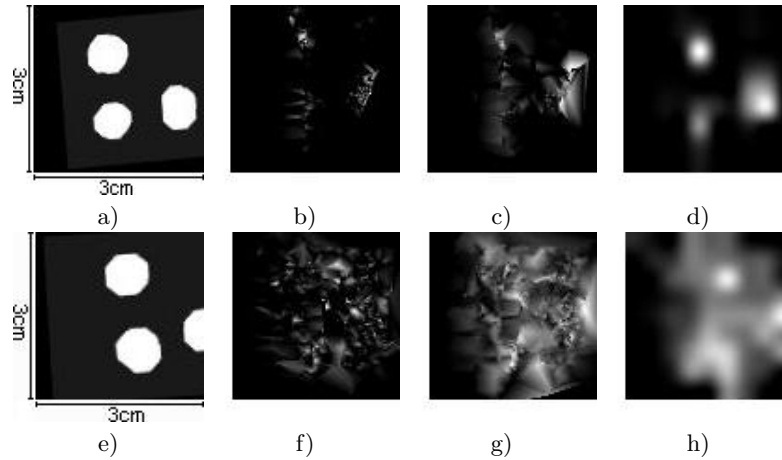
There are, however, several considerations for this new approach. The first point is the implicit assumption that the region to be scanned does neither move nor deform during the scan. Movement and deformation of anatomy after the

Without background						
	NCC			NMI		
	statistical filter	raw data	time filter	statistical filter	raw data	time filter
mean	0.76	0.51	0.35	0.86	0.98	0.99
std	0.05	0.07	0.08	0.03	0.0	0.01
min	0.70	0.40	0.24	0.83	0.97	0.98
max	0.82	0.58	0.46	0.9	0.99	0.99

With background						
	NCC			NMI		
	statistical filter	raw data	time filter	statistical filter	raw data	time filter
mean	0.53	0.38	0.28	0.83	0.97	0.99
std	0.08	0.08	0.04	0.09	0.01	0.00
min	0.44	0.29	0.23	0.68	0.96	0.98
max	0.65	0.47	0.35	0.97	0.99	0.99

**Table 1.** The normalized cross correlation (NCC) and normalized mutual information (NMI) between the reconstructed images and the ground truth for the phantom without background radiation.



**Fig. 6.** The images computed from the measurements on the phantom without background radiation (a-d) and with background radiation (e-h). From left to right: ground truth, raw data, time filtering, and statistical filtering.

scan is unproblematic, as the generated images are snapshots of the current situation. Due to the short acquisition time acquiring a new scan is easily possible and the information can be updated when needed. Our group is currently working on these issues, for example detection of deformation and movement that could invalidate the generated images.

Concerns of bringing further equipment to the operation room are nowadays less relevant. In the case of tracking for example, tailored solutions for surgery are commercially available. Simultaneously, costs of such surgical solutions have been continuously decreasing. Furthermore there might be radiation safety issues for the surgical personnel, but as shown by Piert et al. for FDG radio-guided surgery the doses are negligible [6].

Regarding the tracer to be used, it was taken for granted that the tumor residual has an uptake that allows its detection over the background. This is indeed not always the case. In our institution we have thus developed criteria for selecting proper patients, based on the analysis of pre-operative PET imaging. Related to this, a current issue of research is the minimal amount of residual cancer cells that can be detected with a beta-probe. Daghighian et al report that the beta-probe used by them can detect tumor residuals down to 50 [mg] [7]. Updating these limits are subject of research in our group.

As future work we see special potential in including global reconstruction of the radioactivity distribution rather than only doing local statistical corrections targeting higher quality surface images.

In summary, this paper introduces novel ideas for significantly improving the robustness and the statistical quality of radioactive measurements, and thus improving radio-guided resection border control. The proof-of-concept shows that computer-assistance does not only incorporate advanced visualization and guidance into intra-operative procedures, but also supports the process of reliable and robust functional image acquisition.

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