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TECHNICAL REPORT

Development and characterization of a compact hand-held gamma probe system, SURGEOGUIDE, based on NEMA NU3-2004 standards

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Abstract: Using an intra-operative gamma probe after periareolar or peritumoral injection of a radiotracer during surgery helps the surgeon to identify the sentinel, or first, nodal site of regional metastasis in clinically node-negative patients. The pathological analysis of this node can have an important influence on the treatment staging in various cancers. This paper reports the design and performance evaluation of a gamma probe recently developed in our department. The detector unit of this system consists of an 8 mm diameter and 10 mm thickness monolithic CsI(Tl) scintillator optically, coupled to a Silicon Photomultiplier (SiPM) with an active area of 6×6 mm^2, and a single-hole collimator. The unit is shielded using tungsten. The system can operate in three different modes for Tc-99m, I-131, or F-18 isotopes. The following measurements were carried out to evaluate the performance of the probe: sensitivity in air and scatter medium, spatial resolution in scatter medium, angular resolution in scatter medium, and side and back shielding effectiveness. All experiments have been performed based on the NEMA NU3-2004 standard set up. The measured system sensitivities in air and scatter medium (water) are 1700 cps/MBq and 1770 cps/MBq, respectively, both measured at 3 cm from the collimator. The spatial resolution in the scatter medium is about 45 mm at 3 cm distance from the collimator. Also, the angular resolution of the probe is 74° FWHM. Finally, a shielding effectiveness of 99.5% is measured. The results show that the probe can potentially be used for sentinel lymph node localization during the surgery.

Keywords: Intra-operative probes; Gamma camera, SPECT, PET PET/CT, coronary CT angiography (CTA)

Contents

1 Introduction

Breast cancer is one of the most common cancers among women and there are annually a large number of breast surgical operations worldwide for removal of malignant tumors [1]. However, failure in discovery and removal of cancerous sentinel lymph nodes (SLN) will lead to a metastasis of cancer in the patient [2]. The SLN can be defined as the first lymph node on the direct drainage pathway from the primary tumor [3]. As a matter of fact, morbidity can be significantly reduced using sentinel node dissection [4]. The SLN concept, first described for penile cancer [5] and melanoma [6], has recently been applied for early breast cancer staging [7]. Currently, there are various methods with different degrees of accuracy to detect SLN [8, 9]. Gamma probing is one of the main tools that is currently been used for detection and localization of SLN [10, 11] not only in breast cancer, but also in other types of cancers such as melanoma [12–14]. Since right after world war two, surgical probes have evolved into an important and integral part in surgical management of cancer.

Many techniques can be used for intraoperative gamma probe development. Gamma photons can be either directly detected via room-temperature semiconductor crystals with high atomic numbers [15] or indirectly detected by using scintillator crystals [16]. For indirect detection, scintillator crystal converts gamma photon energy into light photons. The light output readout can be performed by a photomultiplier tube (PMT) or PIN diode. PMT requires high-voltage supply and leads to bulky and sensitive-to-magnetic field probes. The use of PIN silicon photodiodes allows to build compact probes without high voltage supply, low sensitivity to magnetic field, and signal amplitude weakly dependent on temperature changes. Nowadays, most commercially available intraoperative gamma probes are built using a semiconductor [Cadmium telluride (CdTe) or Cadmium zinc telluride (CdZnTe)] [15] or scintillator detector [thallium-activated cesium iodide (CsI(Tl)) or thallium-activated sodium iodide NaI(Tl)] [17]. Direct detection offers very good energy resolution, but the detection efficiency is low, while the indirect detection presents high efficiency and low energy resolution.

A limitation of intra-operative probes using PMT is the size of the PMT (1 cm diameter and 5 cm long). Although CdTe, PIN diode, or CdZnTe all have compact sizes, they are all low gain, noise sensitive, and have low efficiencies for absorption of gamma rays. As a further alternative it is proposed that a SiPM or other solid state photomultiplier (SSPM) devices be used for detection of scintillation light of CsI(Tl) or NaI(Tl) scintillators that have high densities and therefore high absorption efficiencies for 140 KeV gamma rays [18].

The SiPM has high gain and moderate PDE (~20%), very similar to the PMT, but has the physical benefits of compactness, ruggedness and magnetic insensitivity in common with the PIN and avalanche photo diode (APD). In addition, the SiPM achieves its high gain ($1e^6$) with very low bias voltages (~30 V) and the noise is almost entirely at the single photon level. Because of the high degree of uniformity between the microcells, the SiPM is capable of discriminating the precise number of photoelectrons detected as distinct, discrete levels at the output node. The ability to measure a well resolved photoelectron spectrum is a feature of the SiPM which is generally not possible with PMTs due to the variability in the gain, or excess noise. Despite the fact that the SiPM is sensitive to single photons, its dark count rate of $\sim$100 kHz/mm^2 at room temperature [19, 20].

A wide range of probe systems are available with different detector materials, detector sizes and collimation [21–24]. The basic physical performance of a gamma probe for a successful identification of sentinel nodes during the surgery can be described by its sensitivity, side and back shielding, angular resolution, and spatial resolution [21]. The sensitivity is important for detecting nodes which are deep-seated or where the tracer uptake is low; spatial resolution and angular resolution are required for the detection of nodes close to each other or close to the injection site; proper shielding is the key factor in preventing radiation from unwanted locations or body organs from interacting with the detector and producing wrong counts. A fair comparison of probes is only possible, when they are evaluated against key performance metrics. However, since various methods may be used for performance assessment of gamma probes [22, 25], such a comparison gives us little insight into the relative performance in localizing SLN. The NEMA NU3-2004 protocols were published [26] to provide a standard to evaluate and compare the performance of different gamma probe configurations in a situation mimicking a sentinel node surgery in cancer staging.

In this work, we report on the performance characteristics of a newly-developed surgery gamma probe system, SURGEOGUIDE, based on the NEMA NU3-2004 standard.

2 Material and methods

2.1 Gamma probe design

We have developed SURGEOGUIDE, which is a gamma probe system dedicated to SLN identification in breast cancer patients. The probe system consists of a probe head with its associated electronics, encapsulated in an ergonomic housing, a control unit, and the cable connecting the probe to the control unit (figure 1a). The probe head is comprised of an 8-mm diameter and 10 mm thickness (CsI(Tl)) scintillation crystal, coupled to a SensL MicroFM-60050-SMT SiPM, with a 6 mm × 6 mm active area [20]. While the probe is primarily optimized for use with 140-keV gamma rays (the dominant gamma energy of Tc-99m, it can also be used for gamma-ray energies between 60 keV (Am-241) and 364 keV (I-131).

The SiPM's photon detection efficiency (PDE) peaks at 500 nm, which is a good match for CsI(Tl) emission spectra peaking at 550 nm [20, 27]. The detector is equipped with a pinhole tungsten collimator with a 7.5 mm hole diameter and 3 mm length. The detector is shielded by 3 mm thick tungsten for side and back shielding. The probe and associated electronics are placed in a machined housing made of stainless steel (figure 1b). The probe length is 21.5 cm with a tip diameter of 16 mm (figure 1b). The probe weight is 185 g.

Dedicated electronics were developed for signal conditioning and data acquisition, which are placed inside the hand grip of the probe (figure 1b) and control unit (figure 1a). The front-end board provides a 29.5 V bias voltage for the SiPM. The pre-amplification of the signal is performed inside the probe as shown in figure 2a. A typical pre-amplified signal is shown in figure 3. The signal is further amplified in the main board located in the control unit to compensate for cable attenuation and then the single-ended signal is converted to a differential signal (figure 2b). The differential signal is digitized with a high-speed analog-to-digital converter (12-bit ADC, AD9224 (Analog Devices, U.S.A.)) with 25 MHz sampling rate to obtain the full bandwidth of the signal.

2.2 Performance evaluation

Performance characteristics of the gamma probe were measured using the NEMA NU3-2004 [26] protocol. For each test, according to NEMA's instruction, we used two radiation sources: a Tc-99m solution which has been created in a form of a point-like source in a 1 mm diameter capillary tube using some rubber-like silicon paste to confine the activity volume, and a 20 μ Ci Co-57 point-like source. The activity amounts to a volume of approximately 1 mm^3 placed in the center of a 16 × 10 × 10 mm^3 Plexiglas housing.

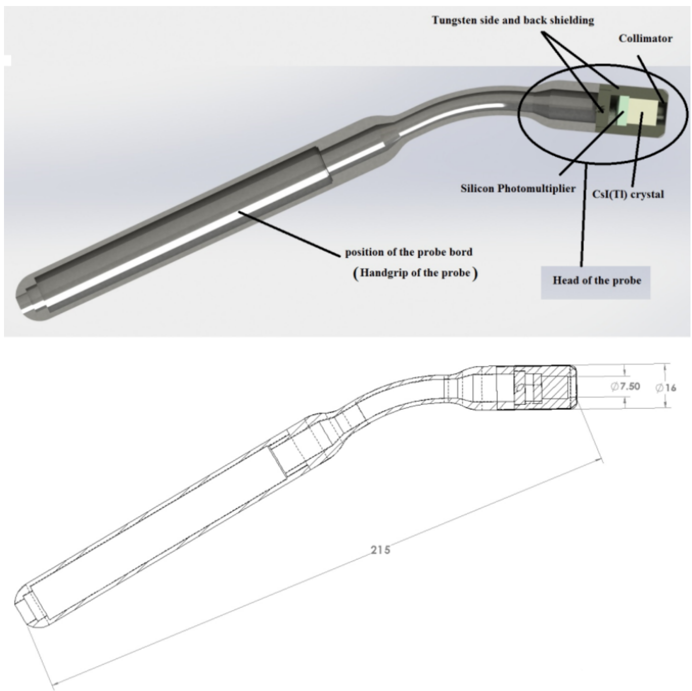
2.2.1 Sensitivity in air

For sensitivity measurements, the Co-57 source was aligned with the central axis of the field of view (FOV) in front of the probe tip. Although according to the NEMA protocol, measurements with source distances between 30 mm to 50 mm are enough for sensitivity evaluation, we measured the sensitivity for source distances ranging from 0 mm to 50 mm with 10 mm steps. The source-to-probe centerline was at least 50 mm far from any scattering material. More than 10,000 counts were recorded for each position. The sensitivity in air was then calculated as the number of counts per second per unit of radioactivity at a specific distance.

2.2.2 Sensitivity in the scatter medium

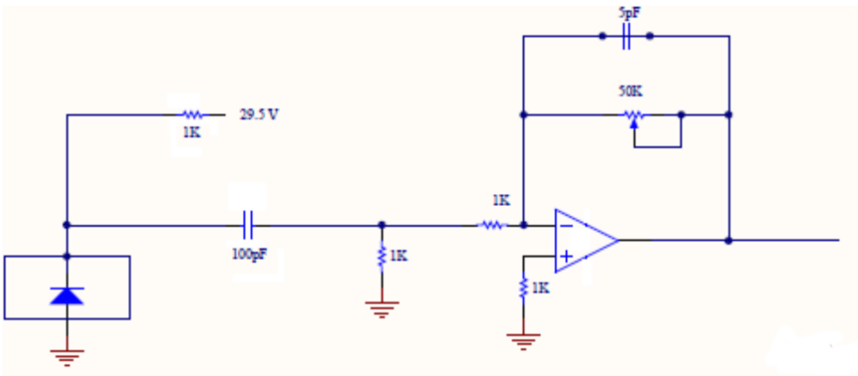
The sensitivity in the scatter medium was measured in a 25 cm × 25 cm × 20 cm container filled with water (figure 4), where the Co-57 source is placed at 10, 20, 30, and 50 mm depths. The probe was positioned such that its tip touches the water surface. The point source was placed along the central axis of the probe. For each position, at least 10,000 counts were recorded. The sensitivity in the scatter medium was calculated as the number of counts per second per unit of radioactivity at a specific distance.

(a)

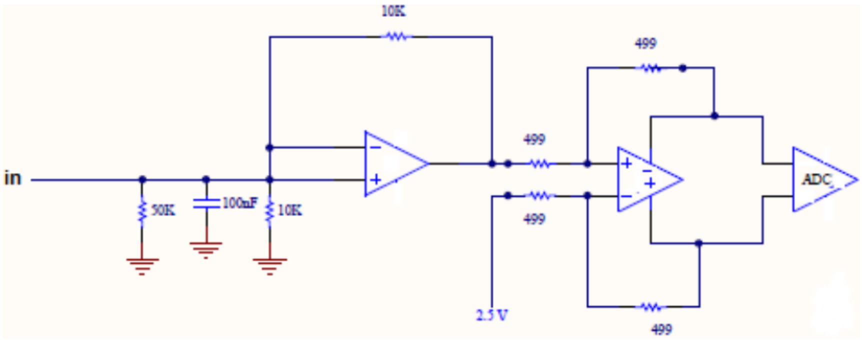


(b)

Figure 1. The SURGEOGUIDE system (a), and the probe of SURGEOGUIDE indicating its main parts (b).



(a)



(b)

Figure 2. The simplified circuit schematic of the probe electronic board that sets the operational voltage to 29.5 V as bias voltage of the SiPM (a), and the simplified circuit schematic of the main electronic board that amplifies and digitizes the signal using high-speed ADCs (b).

2.2.3 Spatial resolution in the scatter medium

Using the water bath, the probe was clamped such that the tip touches the water surface. The Co-57 source was positioned along the central axis of the probe, 30 mm deep in the water. While staying at this constant depth, the distance between the source and the probe axis was changed from −50 mm to +50 mm using 10 mm steps. The source activity was low enough to produce a count rate within the linear count rate response region of the system. Using the measured data, the spatial resolution in the scatter medium was reported in terms of full-width at half-maximum (FWHM) at 30 mm probe-to-source distance.

2.2.4 Angular resolution in the scatter medium

Using the same setup as described in section 2.2.3, we kept the Co-57 source at a fixed depth of 30 cm and the probe tip was touching the water surface. The probe was clamped and rotated about the center of the probe window in 5° steps. The probe was oriented at different angles from the source in the range of −40° to +40°, so that at least ten points were recorded within the FWHM. For all angles, the source-to-probe distance was equal to 30 mm. At least 5000 counts were recorded at 0°. For each of the other angles, at least 500 counts were recorded. Using the measured data at different angles, the angular resolution was reported in terms of FWHM and full-width at tenth of maximum (FWTM).

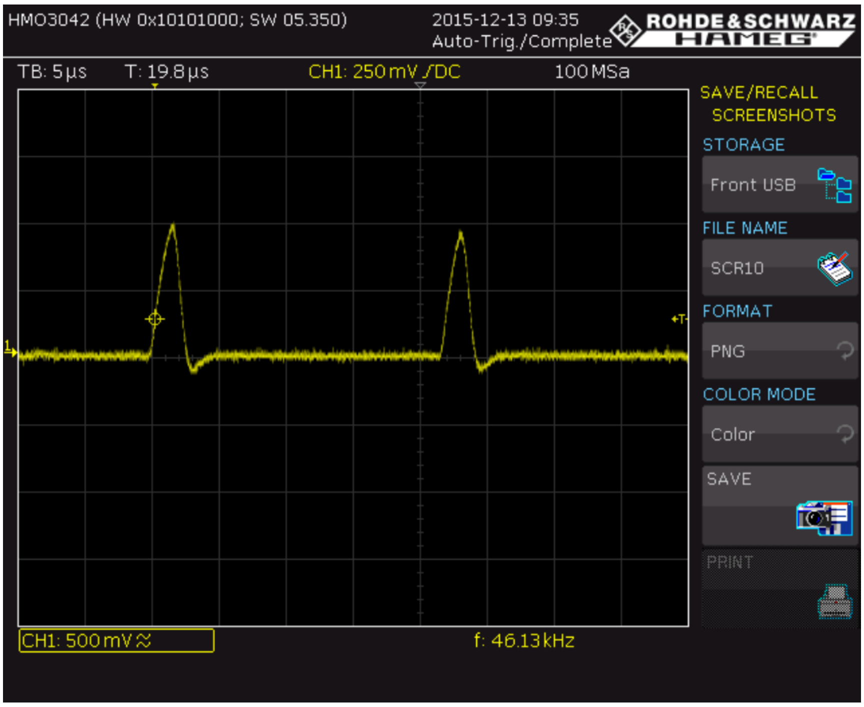


Figure 3. The pre-amplified signal of the probe, measured with oscilloscope.

2.2.5 Side and back shielding effectiveness

We evaluated the side and back-shielding behavior of the probe in air. A Tc-99m point source with an activity of 120 μ Ci was first placed in front of the probe touching the detector surface and then was slowly moved around the entire outer surface of the probe housing, still touching the probe. The maximum observed count rate at each measurement is considered as the corresponding count rate in that position. The side and back shielding was then calculated as count rate per unit of radioactivity using the equations below:

$$\text{Shielding Effectiveness (\%)} = \frac{\text{CPS}_{\text{Axis}}/\,A_{\text{cal}} - \text{CPS}_{\text{Leak}}/\,A_{\text{cal}}}{\text{CPS}_{\text{Axis}}/\,A_{\text{cal}}} \tag{2.1}$$

$$\text{Leak Sensitivity (\%)} = \frac{\text{CPS}_{\text{Leak}}/\,A_{\text{cal}}}{\text{CPS}_{\text{Axis}}/\,A_{\text{cal}}} \tag{2.2}$$

Where CPS_{Axis}, CPS_{Leak} and A_{cal} denote the count rate when the source was placed in front of detector surface, the count rate when the source was moved around the detector, and the activity of the source, respectively.

3 Results and discussion

The results related to performance evaluation of the gamma probe based on the NEMA NU3-2004 protocol are summarized in table 1. The data is normalized to the source activity and corrected for the radioactive decay.

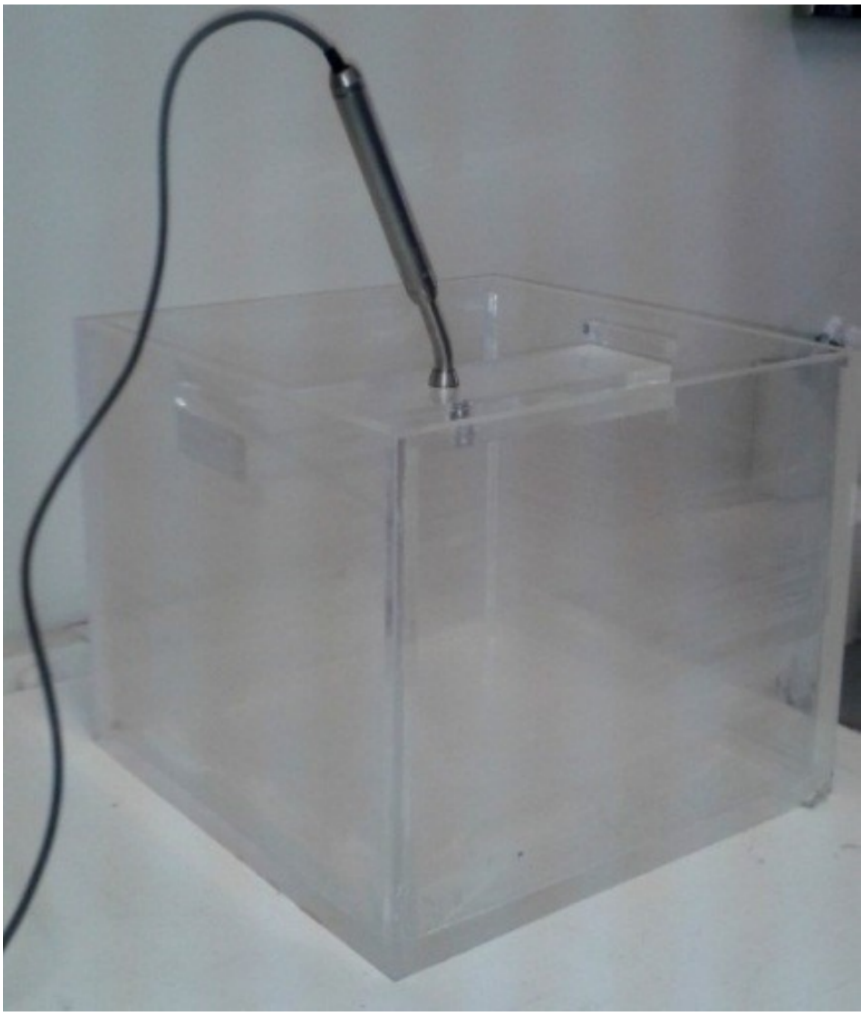


Figure 4. The measurement set-up for the evaluation of the spatial resolution and sensitivity in a scatter medium using a water bath with the size of 25 cm × 25 cm × 20 cm.

Table 1. SURGEOGUIDE performance parameters measured experimentally based on the NEMA NU 3-2004 protocol.

Sensitivity in air (cps/MBq)	at 30 mm	1770
	at 50 mm	920
Sensitivity in scatter medium (cps/MBq)	at 30 mm	1700
	at 50 mm	880
Spatial resolution in scatter medium FWHM		45 mm
Angular resolution in scatter medium FWHM		74°
Side and back shielding	Shielding Effectiveness (%)	99.5
	Leak Sensitivity (%)	0.5

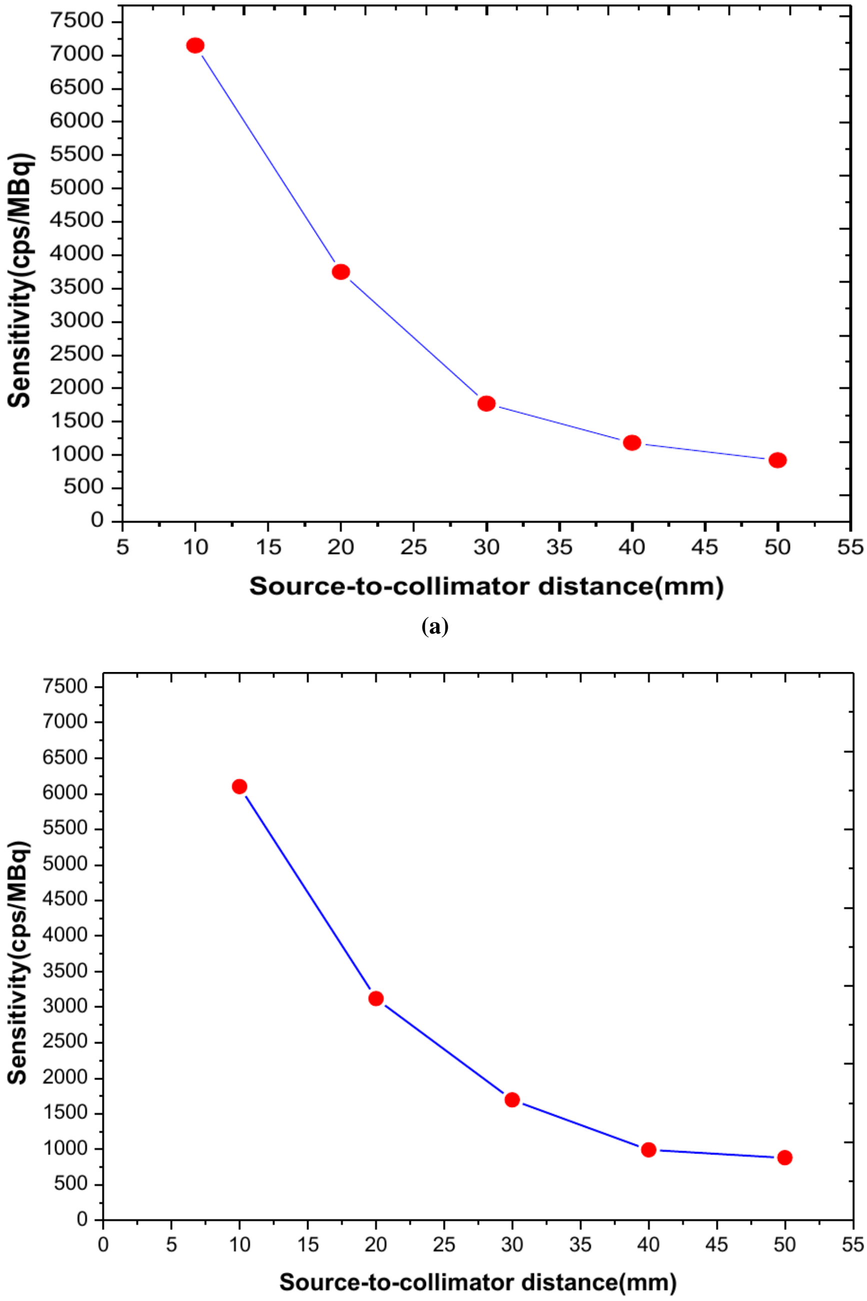


Figure 5. The sensitivity of the SURGEOGUIDE in air (a) and in the scatter medium (b) as a function of the source to collimator distance.

As shown in figure 5a, the sensitivity of the system in air was measured as 7150, 3750, 1770, 920 cps/MBq in 10, 20, 30 and 50 mm distance from the source, respectively. The sensitivity of the system in the scatter medium was also measured as 6720, 3120, 1700, and 880 cps/MBq in 10, 20, 30 and 50 mm distance from the source, respectively (figure 5b).

Probe sensitivity is of great importance for the detection of low-uptake or deep-seated lymph nodes. Since the depth of the sentinel nodes in the body is on average about 3 cm [28–32], the gamma probe should provide high enough sensitivity for 3 cm range in order to provide useful information about the SLN in a practical acquisition time. The sensitivity of SURGEOGUIDE was measured at 1700 and 1770 cps/MBq in the scatter medium and air at 3 mm distance from the collimator, respectively (figure 5a and 5b). The energy window of the system is set to 40%. As a result, most of the scattered radiation is not rejected. So, the sensitivity in the scatter medium has a smaller decrease than the sensitivity in air and the system is less sensitive to scattered gamma rays.

Figure 6a and 6b show the spatial resolution and angular resolution profiles in the scatter medium for a point source at 3 cm depth, respectively. Figure 6c depicts the measured spatial resolution (in terms of FWHM) as a function of the distance from the collimator surface.

High spatial resolution of the gamma probe is helpful in accurately identifying lymph nodes close to each other and also the nodes around the injection site [14]. Spatial resolution and sensitivity are highly dependent on the characteristics of the collimator and the crystal [33]. Since improving one of these parameters results in worsening the other, the sensitivity and spatial resolution of gamma probes should be optimized regarding a specific clinical application [14]. The results show that the spatial resolution and angular resolution in the scatter medium were 45 mm and 74 degree at 30 mm distance from the source, respectively. As shown in figure 6c, the spatial resolution of the SURGEOGUIDE worsens when increasing the distance between the source and the collimator, because the probe's FOV increases with increasing distance [34, 35].

The detector shielding effectiveness and leak sensitivity were calculated to be 99.5% and 0.5%, respectively. Maximum shield leakage was measured on the backside of the detector.

The shield leakage for the gamma probe is important, because such systems could be used in close contact with and even inside the patient's body. Weak shielding may result in detecting unwanted photons from locations not in the FOV of the probe, but from its side or back, leading to an indication of wrong signal for the surgeon that there is a hot node in front of the probe [14, 36, 37].

An appropriate probe for clinical use is the one with high sensitivity, enough shielding and high spatial and angular resolution [38]. However, no single probe can have optimal values for all of the mentioned parameters; for instance, there is an intrinsic compromise between sensitivity and spatial resolution, using the pinhole collimator. Therefore, it is reasonable to assume that the best gamma probe is the one having the best compromise of the performance parameters for a specific application. In this view, the best trade-off depends strictly on the type of radio-guided surgery that is planned. For example, when the predominant use of the gamma probe is for the SLN biopsy in patients with breast cancer or with melanoma, the most important parameter for target detection is sensitivity [39, 40]. In fact, it is crucial for the gamma probe to be able to detect lymph nodes with low uptake. On the other hand, high spatial resolution, although desirable, is relatively less important than sensitivity for SLN procedures, especially in surgical protocols including complete removal of all hot sentinel nodes. The NEMA standard provides a uniform platform for comparing various gamma probes regarding their performance parameters.

Table 2 shows a comparison of SURGEOGUIDE's measured performance parameters with some other commercially available systems. Europrobe (Euromedical Instruments, France) is a gamma probe system whose "large" probe consists of round CsI(Tl) crystal with 5 mm diameter and 10 mm thickness coupled to a $5 \times 5\,\mathrm{mm}^2$ SiPM photodiode. It has a sensitivity of 1900 cps/MBq (in air at 3 cm), 45 mm spatial resolution (FWHM), 102° angular resolution (FWHM), and 0.17 maximum side and back shielding leakage [25]. Although, the SiPM in SURGEOGUIDE is larger,

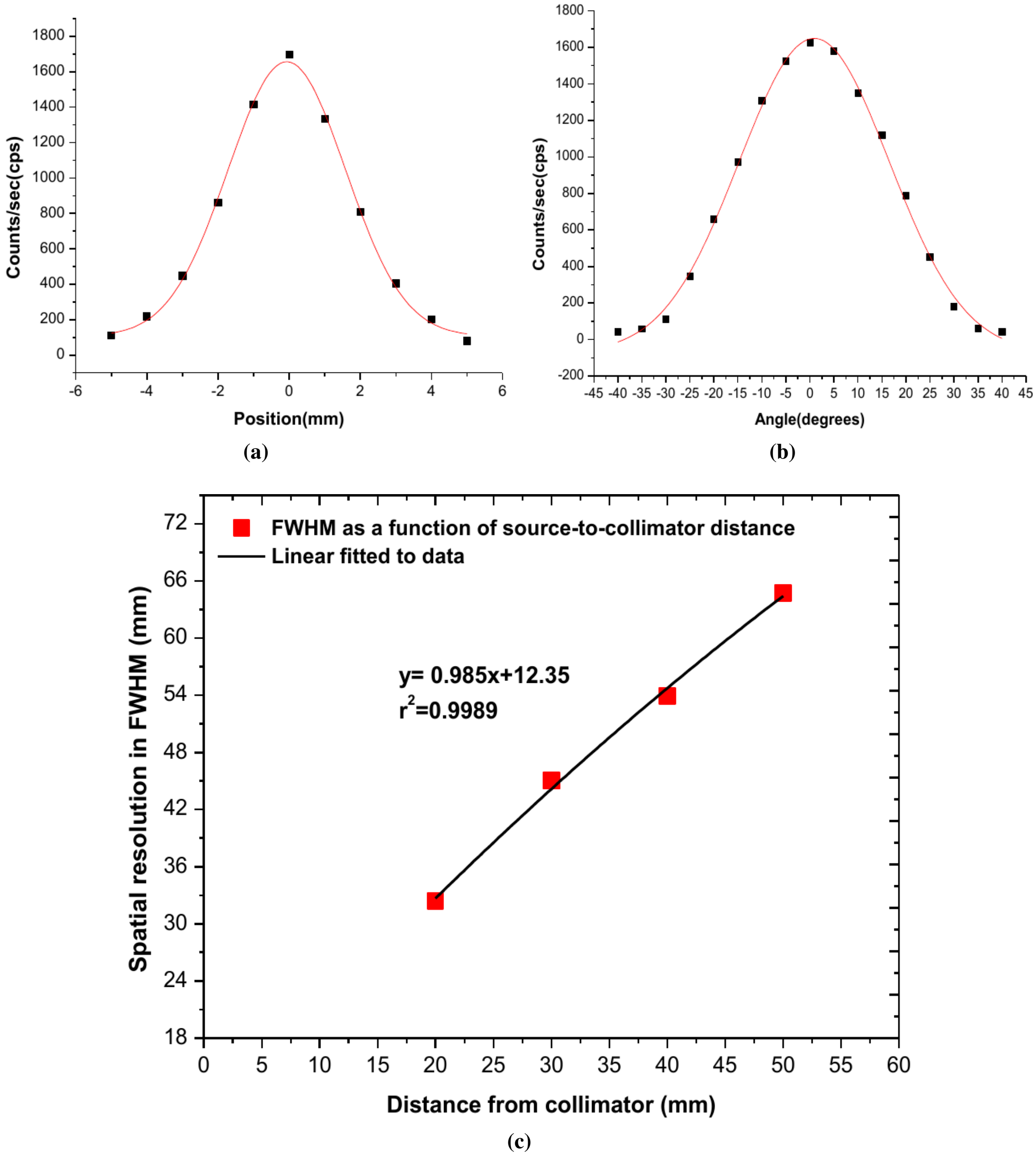


Figure 6. Spatial resolution profile of the SURGEOGUIDE for a point source at 30 mm depth in water (a), angular resolution profile of the SURGEOGUIDE for a point source at 30 mm depth in water (b) and spatial resolution (in terms of FWHM) as a function of distance from the collimator surface (c).

Europrobe achieved better sensitivity probably due to having a larger acceptance angle (angular resolution of 102°). This is due to geometry of collimator which it has caused a lower angular resolution and spatial resolution. Europrobe small probe is based on CdTe with dimensions of $5 \times 5 \times 3\,\mathrm{mm}^3$. It has a sensitivity of 420 cps/MBq (in air at 3 cm), spatial resolution of 39 mm, and angular resolution of 90° [25]. C-Trak gamma probe (Canberra, US) is based on CsI(Tl) and PMT readout. This system is equipped with a collimator with diameter of 6.8 mm. The

Table 2. NEMA Performance parameters of the SURGEOGUIDE in comparison to some commercially available gamma probes [25].

Manufacturer and type		Detector type	Tip diameter/ aperture diameter	Weight (gr)	Sensitivity in air (cps/MBq) at 3 cm	Spatial resolution FWHM (mm)	Angular resolution FWHM (degrees)	Side and back shielding maximum leakage (%)
SURGEOGUIDE (this study)	Large probe	CsI(Tl) SiPM	16/ 7.5	185	1700	45	75	0.5
Europrobe3 (Euromedical Instruments http://www.em-instruments.com)	Large probe	CsI(Tl) SiPM	16/ 5	150	1900	43	102	0.17
	small probe	CdTe	11/ 5	104	420	39	90	0.87
C-Trak (Canberra http://carewise.com/)	Probe with collimator	CsI(Tl) PMT	15/ 6.8	191	1500	28	61	0.02
Navigator (RMD Inc., http://www.dilon.com)	Probe with collimator	CdTe	14/ 7	182	510	35	70	0.9
Neoprobe (Mammotome, http://www.mammotome.com/neoprobe)	Probe without collimator	CdZnTe	14/ 9	142	2200	53	141	0.03

characterization of the system was reported as 1500 cps/MBq (in air at 3 cm), spatial resolution of 28 mm, and angular resolution of 61° [25]. Using a 6.8 mm aperture diameter, the resolution was improved while the sensitivity was decreased in relation to the SURGEOGUIDE. Navigator (Radiation Monitoring Devices, Inc., US) is another gamma probe system based on CdTe detector. The system has a sensitivity of 510 cps/MBq (in air at 3 cm), spatial resolution of 35 mm, and angular resolution of 70°. It uses a CdTe detector with the size similar to the small probe of Europrobe. The results of table 2 show that this system has a lower sensitivity than other systems. As another example, Neoprobe (Mammotome, US) is based on CdZnTe. It has a sensitivity of 2200 cps/MBq (in air at 3 cm), spatial resolution of 53 mm, and angular resolution of 141° [25]. The system has a high sensitivity but angular resolution and spatial resolution is worse than other systems. Because they want to achieve high sensitivity so the Neoprobe has a greater aperture diameter (9 mm aperture diameter). As shown, the SURGEOGUIDE has a comparable spatial resolution and angular resolution with the other probes that do not utilize an external collimator. Side and back shielding of the SURGEOGUIDE is poorer than other systems, since we attempted to decrease its weight and it does not exceed 0.1% of the system sensitivity [21, 26].

While the results of our first prototype system are encouraging, we will continue to improve the system performance for the next generation of the SURGEOGUIDE platform. This includes further enhancement of the convenient using by developing wireless probes and different sets of collimators or probes with different characterization. The presented system can be used for a number of clinical applications including sentinel node detection and radiopharmaceutical-guided surgery. Future work will include various phantom and clinical studies, too.

4 Conclusion

We described in detail the design concept and also performance evaluation procedures of a newly-developed surgery gamma probe system, SURGEOGUIDE, based on the NEMA NU-3 2004 standard. The developed probe using a CsI(Tl) crystal coupled to a SiPM detector showed high performance, while compact and low weight, which is desirable for hand-held devices. The designed gamma probe presented a sensitivity of about 1770 cps/MBq in air and 45 mm spatial resolution, at the depth of 30 mm from the collimator. The lateral leakage was less than 0.5% with internal shielding. These measured performance characteristics of the SURGEOGUIDE showed that it can potentially be used for SLN identification during radiosurgery.

Acknowledgments

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