Surgical Gamma Probe With TlBr Semiconductor for Identification of Sentinel Lymph Node

Fábio E. da Costa, Paulo R. Rela, Icimone B. de Oliveira, Maria C. C. Pereira, and Margarida M. Hamada

***Abstract*—Intraoperative gamma probes have been widely used in surgery oriented to locate the sentinel lymph nodes in breast cancer and malignant melanoma during the surgery. In this paper, a surgical gamma probe using TlBr as a crystal semiconductor detector was developed. The performance of the probe with a maximum sensitivity of 10 cps/kBq and 11 mm of spatial resolution in 10 mm depth shows that the TlBr crystal is suitable to be used in a sentinel lymph node gamma probe. The final probe size was 12.7 mm diameter, 170 mm long and the detection performance met the necessary requirements to be used in radioguided surgery.**

***Index Terms*—Gamma probe, lymph node, thallium bromide.**

I. INTRODUCTION

BREAST cancer is a major health concern for women, and axillary lymph node status is the most important pathological determinant of the prognosis in early breast cancer. The sentinel lymph node is the first lymph node from which the tumor is drained and it becomes involved in metastasis from the tumor [1]. Then, it is required to be located with relatively high spatial resolution, either at the preoperative or intraoperative surgery stage. The spatial resolution (FWHM) should be ≤ 15 mm in head-neck region and ≤ 25 mm in area of groin and axilla [2]. For this purpose, the radioguided surgery technique has been used.

In this technique, the intraoperative localization of the sentinel lymph node is carried out using gamma surgery probes. A radiotracer, such as colloidal suspensions of ^{99m}Tc in human albumin, emitting 140 keV γ -rays, is administered to the patient in the tumor site or close to it before operation, and the radiotracer travels from the tumor to the sentinel lymph node. Then, the probe measures the labeled radioactivity, identifying and locating the sentinel lymph nodes and the visually occult disease, in order to remove it surgically and to proceed to its hystological analysis [1]. Localization and evaluation of sentinel lymph node conveniently radiolabelled by specific tracer is improved by using intraoperative gamma probes having a great sensitivity and accuracy.

TABLE I
MAIN CHARACTERISTICS OF DETECTORS USED IN GAMMA PROBES [5], [8]

Main Characteristics	NaI(Tl)	CsI(Tl)	CdTe	CdZnTe	TlBr
Z	11-53	55-53	48-52	48-30-52	81-35
g.cm^{-3}	3.67	4.51	6.06	5.78	7.56
Energy per electron-hole (eV) at 300 K	-	-	4.43	4.63	5.9

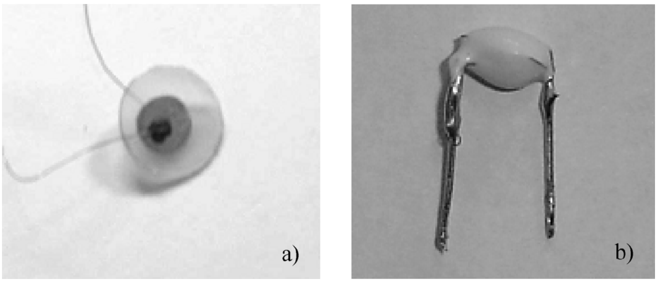

Fig. 1. (a) TlBr crystal view with the gold evaporation and copper wires bounded with coloidal carbon. (b) TlBr detector set completely coated by Araldite glue.

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 [3] or indirectly detected by using scintillator crystals. 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 silicon photodiode (PIN). PMT requires high-voltage supply and leads to bulky and sensitive magnetic field probes [3]. 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 (CdTe or CdZnTe) [4] or scintillator detector (CsI-Tl or NaI-Tl) [2]. Direct detection offers very good energy resolution, but the detection efficiency is low, while the indirect detection presents high efficiency and low energy resolution. It is recommended to use both detectors for an accurate localization of the sentinel lymph node. In the literature, there are several works aiming to develop a suitable probe that presents such characteristics, i.e., good resolution and high detection efficiency.

Due to its high photoelectric absorption efficiency, high density and large band gap, thallium bromide (TlBr) is a good candidate for X-ray and γ -ray spectrometry [5], suitable to measure the gamma ray emission of ^{99m}Tc, and a promising material for room-temperature detectors. Because of these characteristics, TlBr has potential to be used as an efficient and thin detector with the thickness less than 1 mm at 140 keV. In addition, TlBr melts at relatively low temperature (460 °C) [6] and can be

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The authors are with the IPEN/CNEN-SP, Cidade Universitária, 05508-900 São Paulo, Brazil. (e-mail: mmhamada@ipen.br).

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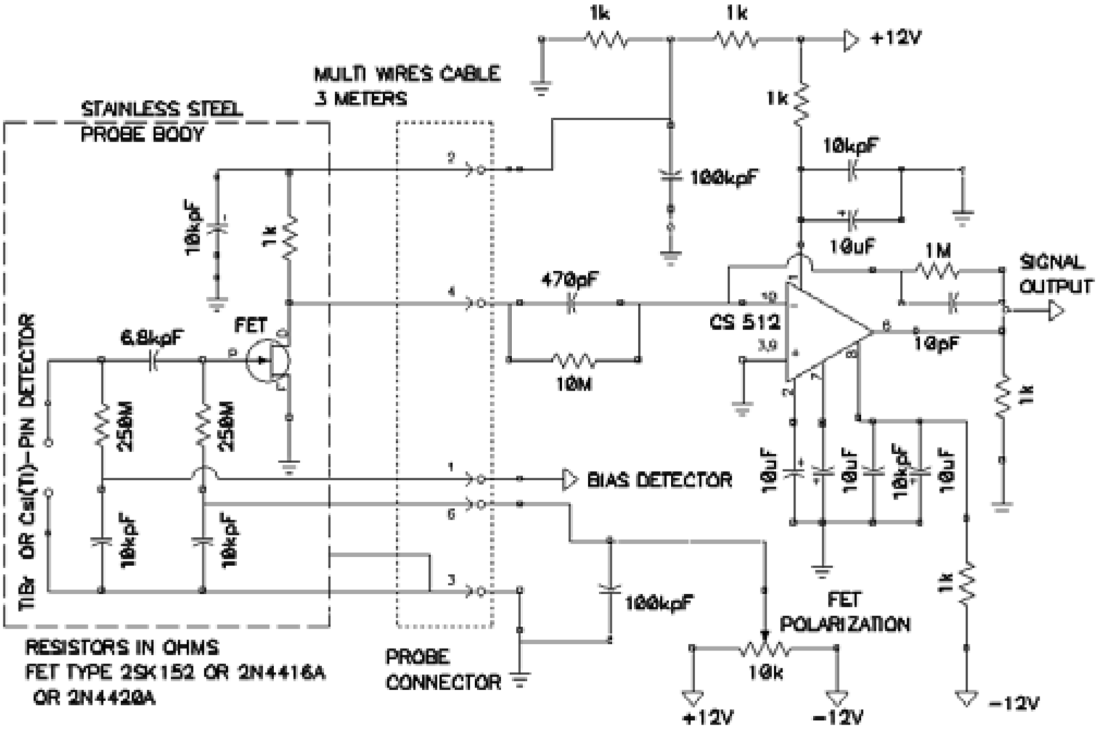

Fig. 2. Schematic diagram of voltage preamplifier. The components inside the dashed rectangle are inside the probe body. The other components are mounted in an auxiliary box.

grown in vacuum or atmospherical pressure, while the CdTe or CZT crystals are grown in high pressure ($>$ 80 atm) and high temperature (1150 °C)[7]. Table I shows the main characteristics of the detectors used in gamma probes. In this paper, studies on the use of TlBr crystal, developed and grown in IPEN laboratory, as a detector in a surgical gamma probe, are presented.

II. EXPERIMENTAL

To produce pure TlBr crystals, commercial TlBr material (99.0%) was purified by zone refining process, 50 passes were carried out in a furnace at the speed of 5 cm/h. The purest section of the TlBr ingot was used for the crystal growth by Bridgman method. The crystals were grown with a rate of 1–2 mm/h at 480 °C in a vertical furnace. The crystal was split in several thick wafers with a diamond saw, followed by mechanical polishing. In order to remove damage from the crystal cleavage, wafers surfaces were then etched using 10% bromine–methanol solution and rinsed with methanol [9]. In order to create the active area, each side of the wafer was coated with gold (5 mm circle) by vacuum deposition. A copper wire was bounded on the gold layer with colloidal carbon, shown in Fig. 1(a). These copper wires were soldered to electric leads and the detector set was completely involved by Araldite glue, shown in Fig. 1(b).

Due to the difficulty to obtain a small size charge preamplifier to meet the requirements of a small size dimension for the probe, a voltage preamplifier was developed splitting the circuit between the probe and the processing signal unit, as shown in Fig. 2. The electronic components inside the probe were arranged inside a glass tube, to ensure the isolation between the electronic parts and the stainless steel wall of the probe body.

The developed preamplifier was evaluated, analyzing the signal output from the second half preamplifier, which was connected to an EG&G 450 Ortec Research Amplifier. The measurements were performed adjusting the amplitude gain to 200 and shaping time to 10 μs. The spectrum was analyzed by EG&G A918 Ortec Multichannel, the count rate at the photopeak was obtained by 550 SCA EG&G Ortec and 776 EG&G Ortec Counter & Timer.

To compare the characteristics obtained for the developed TlBr surgical probe, a CsI(Tl) crystal coupled to a photodiode surgical probe was also developed. The CsI crystals with [Tl] of 1.0×10^{-3} M used in this paper were grown at IPEN using the vertical Brigdman method, with a quartz crucible in vacuum atmosphere [10]. The CsI(Tl) crystal was cut in the dimension of $5 \times 5 \times 5$ mm^3 and polished to be coupled to a Hamamatsu S5106 photodiode.

The surgical gamma probes were mounted using part of the developed preamplifier connected to a TlBr detector, with—200 V bias and collecting holes or a CsI(Tl) crystal scintillator coupled to a Hamamatsu S5106 photodiode, with -30 V bias, encapsulated in stainless steel tube.

A lead shield was used, for both probes, to reduce the lateral counting leakage measurement, which can induce to a false orientation of the tumor and to reach the acceptable leakage value [2]. Thus, a lead shield with 2 mm thickness was incorporated inside the TlBr probe involving the detector. For the CsI(Tl) probe, only an internal shield 0.7 mm thick was inserted, requiring additional 1.3 mm thickness of lead shielding outside of the probe. To improve the spatial resolution, a lead collimator, 2 mm thickness and 4 mm internal diameter was set up in front of the crystal detector for both probes. The similar shielding and

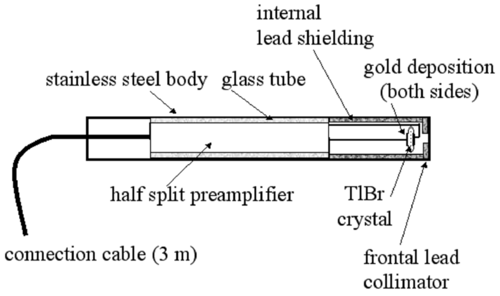

Fig. 3. Schematic diagram of TlBr surgical probe.

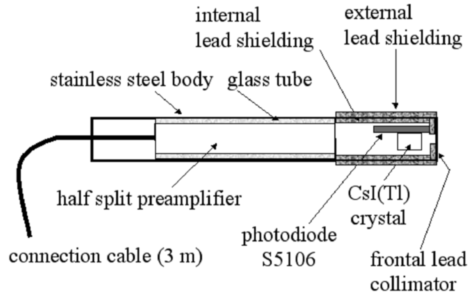

Fig. 4. Schematic diagram of CsI(Tl) coupled to a photodiode surgical probe.

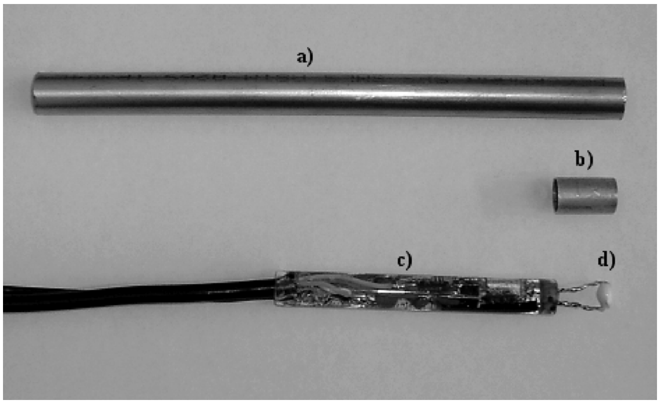

Fig. 5. TlBr surgical probe partially assembled. (a) Probe stainless steel body. (b) Internal lead shielding. (c) Preamplifier assembled inside the glass tube. (d) TlBr crystal.

collimators were used to compare the spatial detection characteristics. Fig. 3 shows a schematic view of the TlBr probe, while Fig. 4 shows a schematic view of CsI(Tl) probe and Fig. 5 the TlBr probe, partially assembled.

The maximum sensitivity of the probe was determined positioning a ^{57}Co radioactive source directly on the probe tip. The spatial resolution is defined as the minimum distance required between two punctual sources in order to identify them as two distinct ones. Then, the spatial resolution was obtained using two $^{99\,\mathrm{m}}$Tc source points, separated 25 mm from each other and covered with a 10 mm thickness acrylic sheet, in order to simulate a tissue equivalent absorption and scattering medium [2]. This configuration is a standard way to simulate two near standing position lymph nodes.

The lateral leakage was measured with 1 mCi radioactive source of $^{99\,\mathrm{m}}$Tc close to the lateral wall of the body probe, in the position that allows a higher count leakage.

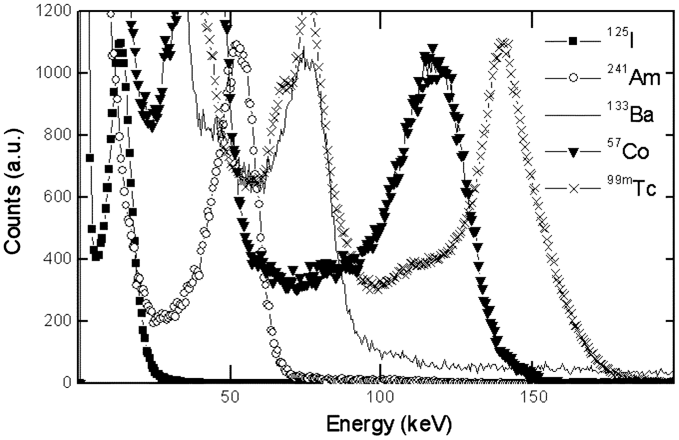

Fig. 6. Energy spectra of the TlBr probe for 27 to 35 keV (^{125}I), 59 keV (^{241} Am), 80 keV (^{133} Ba), 122 keV (^{57}Co). and $^{99\,\mathrm{m}}$ Tc (140 keV).

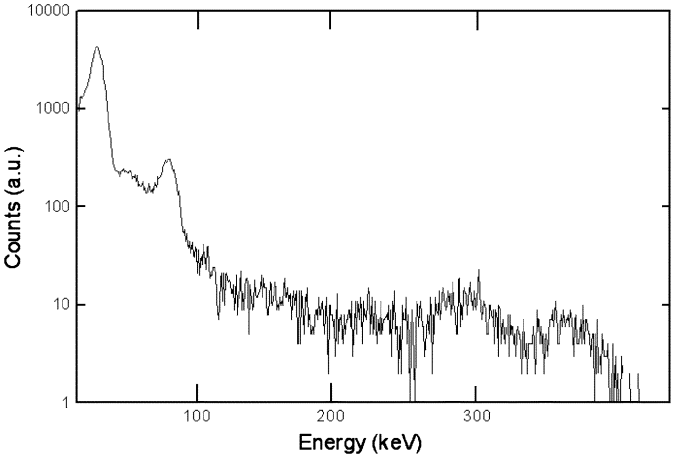

Fig. 7. Energy spectra of the TlBr probe for ^{133} Ba.

III. RESULTS AND DISCUSSION

The final size of the TlBr probe was 12.7 mm of external diameter and 17 mm long, while the CsI(Tl) was 15.3 mm external diameter and 170 mm long

Fig. 6 shows the energy spectra of the TlBr probe for the 27 to 35 keV (^{125}I), 59 keV (^{241} Am), 80 keV (^{133} Ba), 122 keV (^{57}Co), and 140 keV ($^{99\,\mathrm{m}}$ Tc). Fig. 7 shows the energy spectra for ^{133} Ba, in log scale, where the photopeaks in 300 keV and 360 keV can be observed. Fig. 8 shows the energy spectra of the CsI(Tl) probe for the 122 keV (^{57}Co), 140 keV ($^{99\,\mathrm{m}}$ Tc), 300 keV and 360 keV (^{133} Ba), 511 keV (^{22} Na), and 662 keV (^{137} Cs). The energy resolutions are summarized in Table II. The values are compared to that used in conventional charge sensitive preamplifier [3]. The preamplifier integrated circuits, commercially available, present large dimensions to be inserted in probes and they also need additional components. The developed voltage-sensitive preamplifier overlaps this limitation, splitting the preamplifier in two parts, as shown in Fig. 2.

As expected, the TlBr probe showed to be more suitable for lower energy measurements, while the CsI(Tl) is more appropriated for higher energies, as it can be observed in Figs. 6–8. Fig. 9 shows the resolution dependence to the energy for the TlBr probe, and Table II summarizes the energy resolution obtained

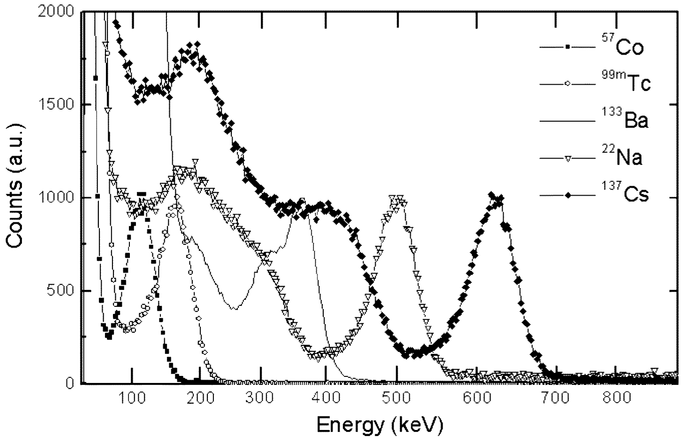

Fig. 8. Energy spectra of the CsI(Tl) probe for 122 keV (^{57}Co), 140 keV ($^{99\text{ m}}$ Tc), 300 keV and 360 keV (^{133} Ba), 511 keV (^{22} Na), and 662 keV (^{137} Cs).

TABLE II
ENERGY RESOLUTION VALUES OBTAINED FOR DEVELOPED TLBR AND CSI(TL) PROBES AND TYPICAL DETECTORS

	RESOLUTION(%)						
	^{125}I	^{241}Am	^{133}Ba	^{57}Co	^{99m}Tc	^{22}Na	^{137}Cs
Energy (keV)	27-35	59	80	122	140	511	662
TlBr	39	24	21	19	18		
CdTe Typical Spectra				5-25[2]			
CsI(Tl)				38	31	14	11
CsI(Tl) Typical Spectra				29[11]	15[3]		8

for both probes. No changes in the spatial resolution and selectivity results were observed for different resolution values. However, probes with higher resolutions showed lower background counting and, as a consequence, points with lower activity can be discriminated more easily. The commercially available intraoperative gamma probe systems have energy resolution in the range of 5%–25% for 122 keV ^{57}Co energy. Kotzassarlidou *et al.* [2] describe that, in clinical practice, poor energy resolution does not lead to significantly poorer lesion detectability. From the graph in Fig. 9, it can be observed that there is a good correlation for energies above 59 keV. The result obtained for 27 keV can be an effect of the electronic noise from the preamplifier that degrades the resolution in this range of energy.

As it can be observed from Table II, the energy resolution is suitable for the application of both developed probes in the radioguided surgery using the most common radioisotope, $^{99\text{ m}}$ Tc (140 keV).

Fig. 10 shows the graph for determination of spatial resolution for TlBr probe, where it can be inferred that the spatial resolution at 10 mm depth is around 11 mm. This result is in accordance with the values required for gamma probes [2]. No significative difference was found for CsI(Tl) probe.

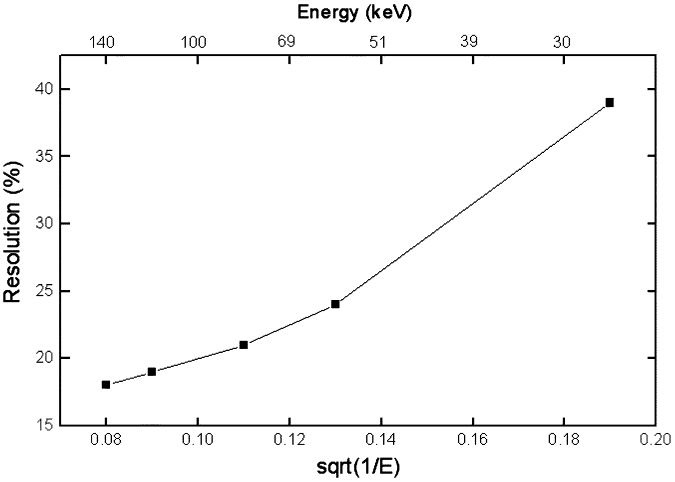

Fig. 9. TlBr probe resolution dependence to the (energy) $^{-1/2}$.

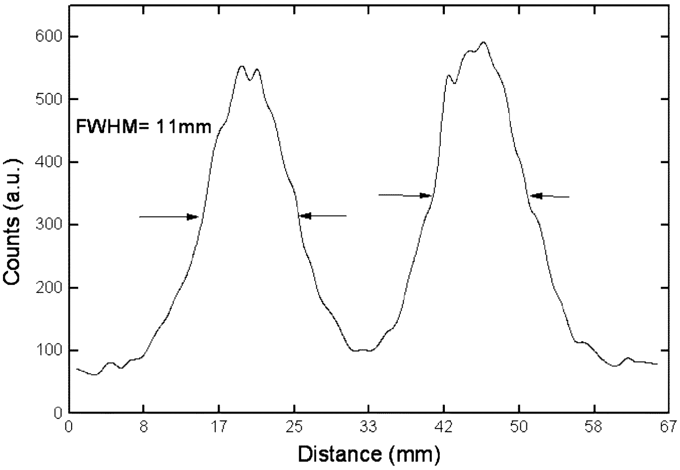

Fig. 10. TlBr probe spatial resolution at the depth of 10 mm, using $^{99\text{ m}}$ Tc sources.

The maximum sensitivity obtained with the probe was 10 and 20 cps/kBq for TlBr and CsI(Tl), respectively. The lateral leakage was less than 0.5% for TlBr probe. The results reach the minimum requirements for gamma probes [2]. For commercial probes, the maximum sensitivity values are between 5 cps/kBq to 100 cps/kBq, medium 30 cps/kBq, however the large difference in the results is due to different diameters, shields, and collimators used in the probes.

Despite the high activity injected in the patient, the lymph node concentrates less than 1% of total activity. As a consequence, the count rate is usually low, then no special attention was given for the dead time during the measurements. The spatial selectivity for the TlBr probe performed at 3 and 30 cm of distance from the source is shown in Fig. 11. Values similar were found for the CsI(Tl) probe.

Both detectors, TlBr and CsI(Tl), presented similar performance. However, it should be emphasized that the TlBr crystal production is in development stage and it is not yet commercially available. The TlBr samples presented a large range of charge collect efficiency from 40% to 85%. The pulse height is strongly dependent on the collect efficiency and the results shown in this work are from a crystal close to 50% efficiency.

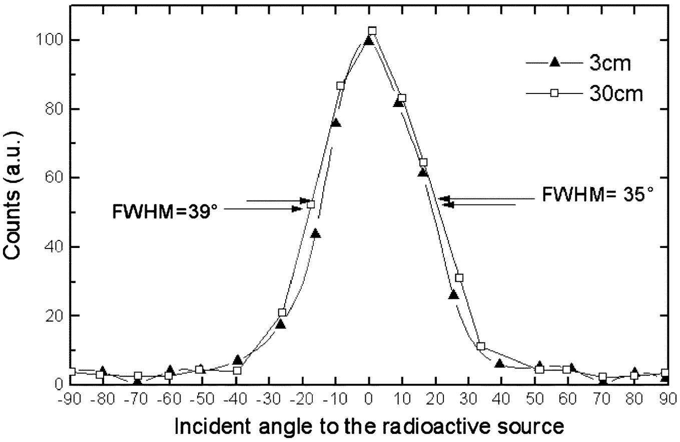

Fig. 11. Spatial selectivity of the TlBr probe at a 3 cm (triangle) and 30 cm (square) distance from the $^{99\,m}$Tc source.

This efficiency is also influenced by polarization effects that acts in different ways for each crystal. During the surgery, the spent time for lymph node identification is short and when the probe is switched off, automatically a positive potential (+12 V) is applied to crystal terminals in order to restore the initial condition, without the polarization effects produced during the use of the probe. Higher sensibility was expected for TlBr than CsI(Tl) crystal probe, but in this work, crystals with 0.3 mm thickness were used, which was not enough to absorb completely 140 keV gamma rays. However, when crystals with more 0.3 mm thickness were used, the collected charge was poor due to higher penetration of 140 keV and the increase of the bias voltage resulted in the detection of high spike production rate.

IV. CONCLUSION

The developed probe using a TlBr crystal showed to be suitable as a sentinel lymph node gamma probe. It presented a maximum sensitivity of 10 cps/kBq and 11 mm for the spatial resolution, at the depth of 10 mm. The lateral leakage was less than 0.5 % with internal shielding. The performance of the TlBr probe was similar to that obtained for the probe using CsI(Tl) crystal with the similar shield and collimator.

The presented performance of the TlBr probe allows to conclude that it is feasible to be used in radioguided surgery and it is also expected that TlBr crystal with better quality can be obtained improving the production technology.

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