

Is the “Ideal” γ -Probe for Intraoperative Radioguided Surgery Conceivable?

Publication in this issue of *The Journal of Nuclear Medicine* of the article by Classe et al. (pages 395–399 (1)) gives the opportunity for some considerations both from a speculative and from a practical point of view about the use of intraoperative γ -probes for radioguided surgery.

After a slow start with the introduction of radioimmunoguided surgery in the 1980s, the last 10 years or so have witnessed a continuous exponential growth in the worldwide use of intraoperative γ -probes. These probes are now used in a variety of radioguided surgical procedures, mostly (but not exclusively) dealing with treatment of malignant disease, such as in the search for sentinel lymph nodes (2–13). This trend has driven manufacturers to develop and introduce to the market several different types of γ -probes, each claimed to be the ultimate, unique solution to the technical difficulties encountered both in wide clinical routine and in experimental clinical protocols.

The features that the nuclear medicine physician and the surgeon should take into account when choosing an intraoperative γ -probe can be defined, considering that the goal of radioguided surgery is to search for (count), detect, and localize hot lesions through a surgical incision of the skin (10). Therefore, an intraoperative probe should first be small and easy to handle, thus allowing minimally invasive surgery whenever adequate. The ergonomic aspects of γ -probes are important also when specific applications are

contemplated; for instance, designing the detecting component on a lateral window rather than on the tip of the probe could be advantageous for applications of radioguided surgery during laparoscopy or thoracoscopy.

Sensitivity is important for detecting hot lesions. It can be defined as the fraction of the emitted radiation that the probe can detect; overall sensitivity is linked to a geometric component (fraction of emitted radiation that intersects the detector, which depends on the solid angle subtended by the probe) and to an intrinsic component (fraction of radiation absorbed within the detector, which depends on the detecting material). High sensitivity allows the detection of low-activity sources.

Spatial resolution and shielding are the key parameters for localizing the source; good spatial resolution allows one to distinguish sources close to each other, as when the sentinel lymph node is close to the radiocolloid injection site. Intraoperative probes are intended for directional counting. In this regard, shielding is important to prevent radiation from unwanted locations from interacting with the detector and producing counts; this parameter is critical mostly when a high background signal is present.

The energy resolution is an important determinant in counting performance, since good energy resolution allows one to recognize and discard scattered radiation based on energy discrimination. Scattered radiation contributes to the blurring of spatial information and spuriously increases background; therefore, it is important to discard counts coming from the scattered component of radiation.

Linearity in energy and counting rate are also desirable to ensure that probes operate optimally in the range of radionuclides and activities used in clinical practice.

The most important physical parameters defining the performance of an intraoperative γ -probe are summarized in Table 1. Obviously, a probe having the highest sensitivity, the best energy resolution (expressed as the percentage FWHM of the photopeak), the best scatter rejection, and the lowest spatial resolution for all radionuclides used clinically would be the probe of choice. Unfortunately, no single probe can have optimal values for each of these performance parameters; for instance, sensitivity and spatial resolution are inversely related to each other. The complexity of these parameters and possible conflict between some of them clearly indicate that it is not possible, either from a theoretic or from a practical point of view, to conceive a γ -probe characterized by the best performance in all parameters. Therefore, it is reasonable to assume that the best γ -probe is generally the best compromise. In this view, it should be emphasized that the best compromise depends strictly on the type of radioguided surgery that is planned. For example, when the predominant use of the γ -probe is for radioguided biopsy of the sentinel lymph node in patients with breast cancer or with melanoma (or with other solid tumors characterized by a high lymphogenic metastatic potential), the most important parameter is sensitivity. In fact, it is crucial to detect with the γ -probe, also, lymph nodes with a low counting rate (10,11). On the other hand, maximum spatial resolution, although desirable, is relatively less important than sensitivity for sentinel lymph node procedures, especially in surgical protocols including complete removal of all hot sentinel nodes. Similarly, probe collimation aimed at restricting the angular field of view of the probe may not be a crucial factor in sentinel lymph node biopsy, at least when the

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TABLE 1
Main Physical Characteristics of an Intraoperative γ -Probe for Radioguided Surgery

Parameter	Definition	Related to	Critical for
Sensitivity (cps/kBq)	Fraction of emitted radiation detected by the probe	Geometry, thickness, effective Z, and density of the detector	Detecting low-activity sources
Spatial resolution (FWHM of PSF, mm)	Ability to accurately define location of a source	Material, size, and lateral shielding of the detector	Localizing sources very close one to each other
Energy Resolution (100 \times $\Delta E/E_\gamma$)	FWHM of the bell-shaped photopeak in the energy spectrum	Material of the detector (number of electrons produced by a radiation in the detector)	Reducing spatial blurring and background due to scattered radiation

FWHM = full width at half maximum height; PSF = point spread function; E_γ = energy photopeak; ΔE = relative energy.

site of radiocolloid injection is distant from the radioactive lymph nodes to be removed. In fact, in this circumstance background radioactivity surrounding the sentinel lymph node is generally rather low. However, collimation becomes important (although possible scatter of radiation by the collimating material could be a confounding factor) when the radiocolloid is injected near the lymphatic drainage basin. An example of this circumstance is injection of the radiocolloid in the upper outer quadrant of the breast (which is close to the axilla), whereby the shine-through effect deriving from radioactivity at the injection site can interfere with correct identification of the axillary sentinel lymph node.

Nevertheless, in other types of radioguided surgery (e.g., minimally invasive parathyroidectomy), the availability of a small γ -probe with good spatial resolution is extremely important. In fact, in this application the tissues adjacent to the parathyroid adenoma (typically the thyroid gland) trap the radiotracer quite efficiently, thus potentially leading to misinterpretation of the intraoperative findings (12). Furthermore, background radioactivity is much higher during radioguided parathyroidectomy than during sentinel lymph node biopsy; therefore, adequate collimation of the γ -probe is crucial for avoiding interference from radioactivity in surrounding tissues. Similar considerations also hold true for radioimmunoguided surgery, as is

done for detecting neoplastic foci in, for example, the abdominal area after injection of radiolabeled monoclonal antibodies. These antibodies, although assumed to be specific for the tumor-associated antigens expressed by tumor cells, are characterized by important distribution in soft tissues with ensuing relatively low target-to-background ratios (3,6,9).

At present the commercially available γ -probes for radioguided surgery can schematically be divided into 2 main categories: scintillation γ -probes and ionization (or semiconductor) γ -probes.

The scintillation probes are based on the principle of light emission due to interaction of the ionizing radiation with a crystal coupled to a photomultiplier, whereas the ionization probes are based on the principle of migration of electric charges induced by the radiation. The most common scintillation γ -probes have a CsI(Tl), NaI(Tl), or bismuth germanate crystal, whereas in the most common ionization γ -probes the constitutive element (the semiconductor) is made of CdTe, CdZnTe, or HgI₂, although many other materials are also used in clinical practice or are under investigation in clinical trials.

Both the scintillation and the ionization γ -probes have advantages and disadvantages, linked to their own physical properties and to the type of planned radioguided surgery.

A large body of experience has been accumulated with the scintillation

γ -probes. The scintillation crystal represents the first and most validated principle for γ -ray detection in clinical practice (especially for imaging, as in γ -cameras), and this is probably the reason that some centers presently consider these probes superior to the semiconductor probes.

The major advantage commonly recognized to scintillation γ -probes is their high sensitivity. In this regard, the sensitivity of the first available semiconductor γ -probes was actually lower than that of the scintillation γ -probes, whereas the semiconductor probes were characterized by better spatial and energy resolutions. However, the more recent reports (1,4-9) seem to show that, mainly because of the availability of new semiconductor materials, the difference in sensitivity between the 2 types of probes is at present very low or negligible. This reduction in the gap between the scintillation probe and the semiconductor γ -probes reflects continuing interest in the development of high-quality devices—development made possible by rapid technologic improvements in the materials used for the semiconductor probes, significantly enhancing quality. Moreover, semiconductor γ -probes are preferred by some users because, generally, they are connected with simpler electronics than are scintillation crystals.

Considering now, specifically, the study by Classe et al. (1), these authors consider sensitivity the most important

parameter in sentinel lymph node biopsy of early breast cancer; therefore, they indicate the bismuth germanate scintillation probe as the optimal choice. We share their view only in part. In fact, even if only this clinical application is considered, special caution should be paid to cases in which the tracer is injected very near the axilla (as occurs for tumors in the upper outer quadrant of the breast). In such cases, the spatial resolution of the probe takes on an important role, possibly even greater than that of sensitivity, in overcoming the problem of high background and scatter activity in the surgical bed. In this regard, semiconductor probes are certainly characterized by higher spatial resolution than are scintillation probes, a feature of special value in procedures such as radioguided parathyroid or abdominal surgery. On the other hand, in the above-mentioned study (1) no significant differences were found in the false-negative rates at sentinel lymph node biopsy when the performance of the 3 γ -probes was compared. These data further support the concept that, at present, the "ideal" γ -probe is the best compromise between physical param-

eters of the probe and specific clinical applications.

Present and future challenges for manufacturers of γ -probes for radioguided surgery are now represented by imaging probes (for which actual size may be the limiting factor for use in minimally invasive surgery) and by positron-detecting probes, given the growing clinical use of tumor-avid positron-emitting tracers.

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