Physica Medica 30 (2014) 340–345

Contents lists available at ScienceDirect

Physica Medica

journal homepage: http://www.physicamedica.com

Original paper

Clinical evaluation of a novel intraoperative handheld gamma camera for sentinel lymph node biopsy

Peter Olcott [a,1], Guillem Pratx [b,1], Denise Johnson [c], Erik Mittra [d], Ryan Niederkohr [e], Craig S. Levin [a,d,f,*]

[a] *Department of Bioengineering, Stanford University School of Medicine, 300 Pasteur Drive, Stanford, CA 94305, USA*
[b] *Department of Radiation Oncology, Stanford University School of Medicine, 875 Blake Wilbur Drive, Stanford, CA 94305, USA*
[c] *St Francis and Franciscan Alliance Hospitals, Indianapolis, IN 46237, USA*
[d] *Department of Radiology-Nuclear Medicine, Stanford University School of Medicine, 300 Pasteur Drive, Stanford, CA 94305, USA*
[e] *Department of Nuclear Medicine, Kaiser Permanente, 700 Lawrence Expressway, Santa Clara, CA 94051, USA*
[f] *Molecular Imaging Program at Stanford (MIPS), Stanford University, 300 Pasteur Drive, Stanford, CA 94305, USA*

ARTICLE INFO

Article history:
Received 11 April 2013
Received in revised form
18 September 2013
Accepted 24 October 2013
Available online 14 November 2013

Keywords:
Gamma camera
Intraoperative imaging
Sentinel lymph node biopsy

ABSTRACT

Objective: Preoperative lymphoscintigraphy (PLS) combined with intraoperative gamma probe (GP) localization is standard procedure for localizing the sentinel lymph nodes (SLN) in melanoma and breast cancer. In this study, we evaluated the ability of a novel intraoperative handheld gamma camera (IHGC) to image SLNs during surgery.
Methods: The IHGC is a small-field-of-view camera optimized for real-time imaging of lymphatic drainage patterns. Unlike conventional cameras, the IHGC can acquire useful images in a few seconds in a free-running fashion and be moved manually around the patient to find a suitable view of the node. Thirty-nine melanoma and eleven breast cancer patients underwent a modified SLN biopsy protocol in which nodes localized with the GP were imaged with the IHGC. The IHGC was also used to localize additional nodes that could not be found with the GP.
Results: The removal of 104 radioactive SLNs was confirmed ex vivo by GP counting. In vivo, the relative node detection sensitivity was 88.5 (82.3, 94.6)% for the IHGC (used in conjunction with the GP) and 94.2 (89.7, 98.7)% for the GP alone, a difference not found to be statistically significant (McNemar test, $p = 0.24$).
Conclusion: Small radioactive SLNs can be visualized intraoperatively using the IHGC with exposure time of 20 s or less, with no significant difference in node detection sensitivity compared to a GP. The IHGC is a useful complement to the GP, especially for SLNs that are difficult to locate with the GP alone.

Introduction

Radiation detection probes have long been used to guide surgery, thanks to their ability to localize and quantify radiopharmaceutical uptake even deep in tissue [1,2]. Currently, the most frequent clinical application of radio-guided surgery is for staging melanoma and breast cancer via sentinel lymph node (SLN) biopsy [3–5]. In this procedure, 20–40 MBq (typically) of a suspension of filtered Tc-99m sulfur colloid or other colloidal is injected intradermally in or around the tumor site [6]. Because the radioactive tracer migrates to the regional lymph nodes that drain the tumor, biopsy of these nodes is useful to predict nodal involvement. Typically, these SLNs have activities ranging from 1 kBq to 1 MBq depending on many factors, including number and size of the lymph nodes in the chain, drainage distance, anatomic location of the nodal basin, and time between tracer injection and surgery.

During surgery, radioactive SLNs are localized with a gamma probe (GP). A GP consists of a radiation detector, often a single scintillation crystal coupled to a photomultiplier tube, and a collimator that only accepts gamma rays impinging within a narrow cone. Hence, a gamma probe does not produce an image. To estimate the shape, extent, or depth of the radiotracer uptake, the surgeon must move the probe around the patient, which can be a source of error. Nodes close to the injection site or with low radioisotope concentration are often indistinguishable from the

---

[*] Corresponding author. Molecular Imaging Program at Stanford (MIPS), Stanford University, 300 Pasteur Drive, Stanford, CA, 94305, USA. Tel.: +1 650 736 7211; fax: +1 650 724 1499.

E-mail addresses: pdo@stanford.edu (P. Olcott), pratx@stanford.edu (G. Pratx), cslevin@stanford.edu (C.S. Levin).

[1] These authors contributed equally to this work.

1120-1797/$ – see front matter © 2013 Associazione Italiana di Fisica Medica. Published by Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.ejmp.2013.10.005

radioactive background. These factors result in longer surgery time and extended dissections to localize occult nodes, especially for complicated cases such as head-and-neck melanoma.

When assessing the performance of a radiation detection instrument, "photon sensitivity" refers to the device's physical ability to detect gamma rays, and "node detection sensitivity" to the overall capacity of the device for localizing SLNs, which combines the physical performance of the device, anatomical factors that challenge localization of nodes, and the skill of the operator (usually a surgeon) in positioning the device and interpreting its output.

We developed a novel intraoperative handheld gamma camera (IHGC) for localizing radioactive SLNs in head-and-neck and other difficult cases. Compared to a GP, the IHGC provides spatial information that can help discriminate focal uptake against diffuse background activity, but it has lower photon sensitivity and a less compact form factor. Therefore, both instruments have complementary qualities and can be used together, the IHGC to image the surgical field and visualize the number and location of radioactive nodes, and the GP to pinpoint the radioactive SLN by direct application against a tissue of interest within the surgical cavity.

Over the last decade, several gamma cameras intended for surgical use have been developed, some of which are now commercially available [2,7]. As shown in Table 1 (adapted from Ref. [7]), these cameras come in different form factors and are based on different detector technologies. Scintillation-based cameras use various scintillators and photodetectors to position gamma events [11–13]. These cameras have good detection efficiency, relatively low cost, but sub-optimal energy resolution. In contrast, semiconductor cameras have higher energy resolution and are more compact but they have lower detection efficiency [8–10]. The reader is invited to consult other review articles for a more comprehensive coverage of this subject [2,7].

Various studies have also been published on the clinical use of small gamma cameras for surgical guidance. One of the earliest clinical studies imaged lymphatic drainage during axillary SLN biopsy in three breast cancer patients using a custom gamma camera [12]. The device was later used in a larger study (138 patients) to show that, for breast cancer patients, intraoperative imaging is not inferior to PLS for detecting and localizing the SLNs [14]. More recent studies suggest that intraoperative imaging is most useful in complicated situations (e.g. anatomic location of the nodes or proximity to the high-activity injection site) [15]. Use of intraoperative imaging was investigated for head-and-neck melanoma [15,16], gynecologic cancers [15], and urologic malignancies [17,18]. The combination of intraoperative gamma imaging with a gamma-emitting seed mounted on a laparoscopic device was also proposed [19]. Another method was proposed to estimate the SLN depth based on the amount of collimator blurring observed in the intraoperative images [20].

Here we report on the first clinical evaluation of a novel handheld, freely moving gamma camera that can image focal uptake in vivo in less than 20 s and typically less than 5 s. Because it is not mounted on a mechanical arm, the IHGC can be placed with greater ease at various angles around the patient. Furthermore, it has a parallel-hole collimator optimized for high photon sensitivity to achieve near-real-time imaging of radioactive nodes and surrounding background.

Methods

Gamma camera

The IHGC was specifically designed for intraoperative imaging (Fig. 1A) [21]. It consists of a parallel-hole lead collimator coupled to a pixilated NaI(Tl) scintillation crystal array, itself coupled to a flat panel, multi-anode Hamamatsu H8500 position-sensitive photomultiplier tube. The collimator is 5 × 5 cm^2 large in area and 1.5-cm-thick, with 1.3 mm hexagonal holes and 0.2-mm septa. The 1.7-mm pitch crystal array is composed of 29 × 29 individual crystals, each 1.5 × 1.5 × 6 mm^3 in size. Approximately 3 mm of lead shielding is wrapped around the five non-imaging faces of the IHGC to protect the detector head from out-of-field activity. The entire camera weighs 1.1 kg.

The performance of the IHGC was measured by imaging a Tc-99m flood source [21]. The intrinsic spatial resolution was found to be 1.8 mm FWHM, and the energy resolution 12% FWHM at 140 keV. The photon sensitivity of the IHGC with its parallel-hole collimator is 270 cps/MBq (point source).

From a physical perspective, the IHGC has higher photon sensitivity than a conventional high-resolution NaI gamma camera ($\sim$180 cps/MBq) but lower photon sensitivity than a typical GP (>5000 cps/MBq). However, the high photon sensitivity of the GP is only achieved when the target is right in front of the single hole of the pinhole collimator, and drops off inversely with the square of the distance between the probe and the target [22]. In contrast, the IHGC has constant photon sensitivity as a function of distance and spatial resolution that increases as the camera is brought closer to the source. Placed almost in contact with the source, the high

Table 1
Characteristics of the IHGC and other intraoperative gamma cameras.

Small gamma camera	Detector	Matrix size	FOV (detector)	Size (detector head)	Weight	Energy range	Collimator
IHGC	NaI (Tl) PS-PMT	29 × 29	50 mm × 50 mm	64 mm × 64 mm × 76 mm	1.1 kg	30–300 keV	Parallel-hole
POCI	YAP (Ce)		⌀ 24 mm		2 kg	Tc-99m, I-125, In-111	Parallel-hole
Minicam®	CdTe	16 × 16	49 mm × 49 mm	⌀ 95 mm height 150 mm		20–200 keV	Parallel-hole
MinicamII®	CdTe	16 × 16	40 mm × 40 mm	70 mm × 170 mm × 250 mm	700 g	30–200 keV	Parallel-hole
LumaGEM	CsI (Na) PS-PMT	16 × 16	20 mm × 20 mm			30–300 keV	Parallel-hole, pinhole
eZ-SCOPE®	CdZnTe	16 × 16	32 mm × 32 mm	60 mm × 60 mm × 220 mm	800 g	71–364 keV	Parallel-hole, pinhole, coded ap.
Second POCI	CsI (Na) IPSD	50 × 50	⌀ 40 mm	⌀ 95 mm height 90 mm	1.2 kg	105–175 keV	Parallel-hole
Sentinella 102®	CsI (Na) PS-PMT	300 × 300	40 mm × 40 mm	8 cm × 9 cm × 15 cm	1 kg	50–200 keV	Pinhole
GE camera	CdZnTe	16 × 16	40 mm × 40 mm	Height 150 mm	1.2 kg	40–200 keV	Parallel-hole
CarollReS	Gd2SiO5 (Ce) PS-PMT		50 mm × 50 mm	78 mm × 78 mm × 275 mm	2.49 kg		Parallel-hole
HRC	CsI (Tl) PS-PMT	20 × 20	49 mm × 49 mm		2 kg		Parallel-hole
MediPROBE	CdTe	256 × 256	14 mm × 14 mm	200 mm × 70 mm × 30 mm	1.5 kg		Pinhole
SSGC (prototype)	CdTe	32 × 32	44.8 mm × 44.8 mm	152 mm × 166 mm × 65 mm	2.7 kg	550 keV maximum	Parallel-hole
SSGC (clinical)	CdTe	32 × 32	45 mm × 45 mm	82 mm × 86 mm × 205 mm	1.4 kg	550 keV maximum	Parallel-hole

Table adapted from Ref. [7].