Radioguided Surgery: Open Issues and Perspectives

Giuliano Mariani
Regional Center of Nuclear Medicine
University of Pisa Medical School, Pisa, Italy

Vienna, July 19-21, 2010
Radioguided Surgery: Definitions

• Complex of pre- and intra-operative procedures that imply interaction of at least due disciplines (Nuclear Medicine and Surgery) with the aim of optimizing oncologic surgery.

• Closely linked to the modern approaches aiming at reducing as much as possible invasiveness of surgery and at sparing unnecessary surgeries also in the oncologic domain.

• Two main application domains:
  - Sentinel lymph node biopsy (solid epithelial cancers)
  - Radioguided occult lesion localization (ROLL).
Radioguidance

Adding "hearing" (proportional to radio-activity accumulation and directed by distribution) as an extra-sense of the surgeon (in addition to "seeing" and "touch"), with incremental value versus conventional preoperative imaging.
Radioguidance

• Utilization of probes for intra-operative detection of radiation ($\gamma$ or $\beta^+$, with or without imaging) emitted by a tissue of interest that has preliminarily been “radiolabeled”.

• Such detection “guides” the surgeon for faster and more accurate identification/localization of the tissue to be removed.
Radioguided Surgery

• **Sentinel lymph node**: Mapping of lymph nodes draining the tumor site, after peri-tumoral administration of a lympho-tropic radiopharmaceutical (non-specific).

• **ROLL**: Localization of a non-palpable/non-visible tumor lesion, after administration of suitable radiopharmaceutical either intra-tumorally (\(^{99m}\)Tc-MAA, non-specific) or systemically (tumor-seeking radiofarmaceuticals).
Sentinel Lymph Node Biopsy

- Breast cancer
- Cutaneous melanoma
- Penile cancer
- Head & neck cancer
- Gynecologic cancers
- Gastrointestinal cancers
- Prostatic cancer
- Non-Small Cell Lung Cancer
- Thyroid cancers
- Others?
ROLL

- Breast cancer
- Parathyroid tumors
- Neuroendocrine tumors
- Solitary pulmonary nodules
- Locally recurring thyroid cancer
- GI cancers (MoAb and $^{99m}$Tc-MAA)
- Bone lesions
- $[^{18}F]$FDG-avid tumors
- Others?
Endoscopic Injection of $^{99m}$Tc-MAA in Colonic Lesions
Laparoscopic Gamma-Probe
Ultrasound-Guided Injection of $^{99m}$Tc-MAA in Locally Recurring Thyroid Cancer

Pisa Group: Ann Surg Oncol (submitted)
Ultrasound-Guided Injection of $^{99m}$Tc-MAA in Locally Recurring Thyroid Cancer

Pisa Group: Ann Surg Oncol (submitted)
# Ultrasound-Guided Injection of $^{99m}$Tc-MAA in Locally Recurring Thyroid Cancer

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean ± SD</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lesions/pt (mean ± sd)</td>
<td>1.7 ± 0.9</td>
<td>1 – 4</td>
</tr>
<tr>
<td>Lesion size, mm (mean ± sd)</td>
<td>11 ± 4.5</td>
<td>4-20</td>
</tr>
<tr>
<td>Size ≤ 10 mm</td>
<td>28/59 (47%)</td>
<td></td>
</tr>
<tr>
<td>Level (Robbins)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>V</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>VI</td>
<td>17</td>
<td></td>
</tr>
<tr>
<td>VII</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

*Pisa Group: Ann Surg Oncol (submitted)*
ROLL with Tumor-Seeking Radiopharmaceuticals

- $^{99m}$Tc-Sestamibi
- $^{111}$In-Octreotide
- $^{131}$I-Iodide
- $^{111}$In-MoAb
- $^{99m}$Tc-Depreotide
- $^{99m}$Tc-Bombesin and other peptides
- $^{[18F]}$FDG
- $^{[18F]}$Fluoro-deoxyuridine
- $^{68}$Ga-DOTA-TOC
- Etc.
15-mm nodule in upper lobe of right lung
CT-guided FNA: undetermined
Radioguided VATS 24 h after $^{99m}$Tc-Depreotide (700 MBq): Adenocarcinoma.
Lesion/background SPECT: 1.8
Lesion/background VATS: 2
Most Recent/Promising Developments in Radioguided Surgery

- Wireless gamma probes
- Hybrid imaging (pre-operative)
- Intra-operative imaging
- Positron-sensitive probes
- Probes for high-energy gamma photons
- Probes with 3-D tracking and optical/radioactivity fusion ("surgical eye")
SPECT/CT with $^{99m}$Tc-Sulfur colloid for sentinel lymph node biopsy
SPECT/CT with $^{99m}$Tc-Sulfur colloid for sentinel lymph node biopsy
SPECT/CT with $^{99m}$Tc-Sestamibi for parathyroid adenomas

Patient #1

Patient #2
SPECT/CT with $^{99m}$Tc-Sestamibi in recurrent primary hyperparathyroidism

Ectopic parathyroid adenoma in upper mediastinum
SPECT/CT with $^{99m}$Tc-Sestamibi in secondary hyperparathyroidism (US: hyperplastic right lower parathyroid)

Multiple-gland disease: lower right, upper right (retro-tracheal), and lower left (para-retro-tracheal)
Radioguided Detection of Cancer

1- Probe for high-energy gamma rays: detection of deep-seated tumors

2- Beta-probe for detection of positrons: checking the margins

Courtesy of IntraMedical Imaging, Los Angeles, Ca
The GF&E design
Electronic Collimation versus Mechanic Collimation
γ-Locator DXI
Pisa: Clinical Case 1
Patient SV, 79-yr old woman

09.04.08: Biopsy left breast

✓ Possible infiltrating cancer (but non-diagnostic)
12.05.08: Lymphoscintigraphy for SLNB

45° Left oblique

SPECT/CT
13.05.08: PET/CT with $[^{18}\text{F}]$FDG

$\text{SUV}_{\text{max}}$ 3.7 (primary lesion in left breast)
**13.05.08: Surgery, about 2 h after $[^{18}\text{F}]$FDG and 24 h after $^{99m}\text{Tc}$-Nanocoll**

**Intraoperative counts**

<table>
<thead>
<tr>
<th></th>
<th>IN VIVO $^{99m}\text{Tc}$</th>
<th>IN VIVO $^{18}\text{F}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>SLN</td>
<td>5500 cps</td>
<td>Tumor 10600 cps</td>
</tr>
<tr>
<td>Background</td>
<td>655 cps</td>
<td>Background 400-500 cps</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>EX VIVO $^{99m}\text{Tc}$</th>
<th>EX VIVO $^{18}\text{F}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 SLN</td>
<td>3000 cps</td>
<td>Tumor 9030 cps</td>
</tr>
<tr>
<td>2 SLN</td>
<td>1051 cps</td>
<td>Background 400 cps</td>
</tr>
<tr>
<td>Background</td>
<td>400-500 cps</td>
<td>Resection bed 400 cps</td>
</tr>
</tbody>
</table>
Intraoperative Histology

- Infiltrating breast cancer (with free margins)
- LNS (1) : micrometastasis
- Axillary dissection
Pisa: Clinical Case 2
Patient CG, 59-yr man

18.06.08 PET/CT: $\text{SUV}_{\text{max}}$ 15.8 in CT-visible lesion at the left lower lobe.
19.06.08: Surgery, 2-3 h after $[^{18}\text{F}]$FDG

**Intraoperative Counts**

- Lesion 4700 cps; ex vivo 2300 cps
- Lingula 1500 cps
- Background 500/600 cps
- Carenal lymph node *in vivo* 800/1230 cps; ex vivo 500 cps
- Hylar lymph node 600/800 cps
- Pulmonary vein 500/600 cps

Surrounding healthy tissue ex vivo 200 cps
Atypical Left Lower Lobectomy (including part of lingula)

Histology

- Moderately differentiated adenocarcinoma (G2), with mixed features (acinar, broncho-alveolare and solid).

- 13 hylar-mediastinal lymph nodes with reactive hyperplasia and anthracosis (but no metastasis).

- Stage: pT2(G2) N0 Mx.
CSS300 for freehand SPECT

Imaging & Navigation by SurgicEye’s CSS300

Gamma Detection using conventional gamma probe

freehand SPECT imaging and navigation device
Spatial localization system of CSS300

1. Handle (can be covered to be used sterile)
2. Optical camera
3. Infrared localization system
4. Non-sterile Handle
Accessories of CSS300

Gamma probe with sterile tracking target

Sterile patient target
Freehand SPECT imaging technology
used in CSS300 during surgery

Data with tracked non-imaging probe
Non-uniform/non-symmetric set
<180° covered
Center depends on scan
< 40 thousand events
Cases of SLNB in Breast Cancer

3D Imaging and Navigation at the Regional Center of Nuclear Medicine, University of Pisa Medical School, Pisa (Italy)
Case 1: pre-incision image / visualization in 3D (focus on 1st SLN)
Case 1: pre-incision image / visualization in 3D (focus on 2 SLNs)
Case 1: image after resection of 1st SLN / visualization in 3D

Injection site

Remaining SLN (2nd)

2nd SLN

Lymphatic / 3rd SLN?
Case 2: pre-incision image / visualization in 3D
Case 2: image after resection of 1st SLNs / visualization in 3D
Case 3: pre-incision image / visualization in 3D

Injection site

SLN

IAEA
Case 3: image after resection of 1st SLN / visualization in 3D