Simposio AIRO-SIRM: Diagnostica per immagini morfologica e funzionale nella stadiazione, terapia e follow-up dei sarcomi delle parti molli

Ruolo dell’imaging nella pianificazione del trattamento

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Imaging in Soft Tissue Sarcoma

- Different tumor sites
  (extremities, retroperitoneum, thorax, H&N)

- Different histologic types
  with different molecular changes and natural history

- Different treatment approaches of RT
  (preoperative/exclusive, postoperative, perioperative, intraoperative)
Morphological Imaging

- Rx
- US
- CT (with contrast)
- MRI (T1 without and with contrast, T2)
Functional Imaging

**Available at present:**

- Increased/decreased content of molecules
  - Active transport of metabolites
  - Passive diffusion of molecules
  - Different concentration of normal molecules

- Different distribution of H2O

- Increased blood flux (angiogenesis)

**Optimal:**

- Specific marker of clonogenic cells
Imaging in Radiation Oncology

Patient selection
- Workup
  - Predictive and Prognostic value

Radiation planning
- Target (and non-target) delineation
- Dose painting
- Adaptive RT
- Verification of RT (QA)

Patient outcome
- Assessment of response
- Detection of recurrence
- Radiation Therapy Process
768 pts treated with surgery + RT pre/post based on CT + diagnostic CT and MRI
7.8% developed local recurrence
- 6.4% in field
- 1.1% out of field
- 0.3% marginal

The proportion of LR patients that received either preoperative RT alone (50 Gy), or postoperative RT (60-66 Gy) was nearly equivalent (6.9% and 6.4% respectively)

Conclusions: The majority of STS tumors recur in field, indicating that the incidence of LR may be affected more by differences in biologic and molecular characteristics rather than aberrations in RT dose or target volume coverage. In contrast, only two patients relapsed at the IRV boundary, suggesting that the risk of a marginal relapse is low when the TV is appropriately defined. These data support the accurate delivery of optimal RT volumes in the most precise way using advanced technology and image guidance. © 2012 Elsevier Inc.
**IMRT vs. 3D-CRT**

(Hong et al, Int J Rad Oncol Biol Phys, 2004)

**Significant sparing by IMRT:**
- Intestinal cavity
- Stomach
- Contralateral kidney

(Paumier et al, Radiother Oncol, 2011)
Gross tumor defined by MRI T1 plus contrast images (MRI with contrast is required). Fusion of MRI and CT is recommended to delineate the GTV for radiotherapy planning. Intravenous contrast is recommended, particularly for upper extremity lesions, where there is a greater rotational mobility, and positioning fidelity between the diagnostic MRI and the planning CT may be more difficult to achieve.
Include gross tumor and clinical microscopic margins (CTV = GTV plus 3-cm margins) in the proximal and distal directions. If this causes the field to extend beyond the compartment, the field can be shortened. The radial margin from the lesion should be 1.5 cm, including any portion of the tumor not confined by an intact fascial barrier, bone, or skin surface. The suspect edema (MRI T2) is often included. However, clinical judgment is required to make sure whether the above margins need to be extended to cover the T2 edema defined on MRI T2 images.
**Conclusions:** Almost perfect agreement existed in the GTV of these two representative cases. There was no significant disagreement in the CTV of the lower extremity, but variation in the CTV of upper extremity was seen, perhaps related to the positional differences between the planning CT and the diagnostic MRI.

*(Wang et al, Int J Radiat Oncol Biol Phys, 81:775-80, 2011)*
Target for pre-operative RT
(Haas et al, 2012)

GTV: T1(contrast)-MRI + CT

CTV: GTV + 1.5 cm radially and 4 cm longitudinally including edema
Assessed MRI and pathology in 15 STS patients undergoing surgery.

Tumor cells beyond main mass in 10/15:
- 6 pts < 1cm
- 4 pts 1-4 cm, in 9/10, in area of T2 edema, which was usually proximal/distal to tumor

Recommended 4 cm margin
Are all sarcomas alike in their potential to microscopically invade surrounding tissues?

- **Growth Pattern “pushing borders”** (well differentiated liposarcoma ben differenziato) → rare microscopic foci at distance

- **Growth Pattern with aggressiveness** (high mitotic index, genetic mutations, lympho-vascular infiltration) → frequent microscopic foci at distance (dermatofibrosarcoma protuberans, aggressive fibromatosis, subcutaneous myxofibrosarcoma)

(Haas et al, 2012)
Target for post-operative RT
(Haas et al, 2012)

Imaging: CT and MRI, T2

CTV: surgical volume + 1.5 cm radially and 4 cm longitudinally, if R0 < 4 cm (no bone, fasciae and joints)

Boost: same as CTV except in the longitudinal direction where 2 cm margin are considered
Non-target Structures: Saphenous Volume
(Liss et al, ASTRO 2012)

131 pts

Pts with higher total volume of saphenous vein is associated with development of late edema in the lower extremity

A trend of higher dose to the saphenous vein was also associated with this late effect
Dose Painting?
FDG PET/CT

- Sensitivity 90-95%, specificity 85-90%
- May help determine high vs. low grade
- May predict pathologic response
- May be helpful in recurrences

Open issues:
- How to define positivity (SUV>2?)
- How to outline on PET images (visual method, SUV value, SUV%, SBR, specific algorithms)

Figure 1. FDG-PET imaging of a patient with a large retroperitoneal sarcoma. The image demonstrates significant heterogeneity in tumour FDG uptake.
FDG-PET Dose Painting

PET/CT image with SUV-based contours

T1-Gd enhanced MRI

<table>
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<tr>
<th></th>
<th>D_{98}% (Gy)</th>
<th>D_{2%} (Gy)</th>
<th>D_{50%} (Gy)</th>
<th>Mean Dose (Gy)</th>
<th>HI</th>
<th>CI</th>
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<td>GTV_{65Gy}</td>
<td>65.2</td>
<td>67.9</td>
<td>66.4</td>
<td>66.4</td>
<td>1.03</td>
<td>0.85</td>
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<tr>
<td>GTV_{60Gy}</td>
<td>60.2</td>
<td>65.1</td>
<td>61.6</td>
<td>62.0</td>
<td>1.07</td>
<td>0.88</td>
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<tr>
<td>GTV_{53.5Gy}</td>
<td>53.6</td>
<td>60.3</td>
<td>55.5</td>
<td>56.3</td>
<td>1.11</td>
<td>0.90</td>
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<td>PTV_{50Gy}</td>
<td>49.7</td>
<td>55.6</td>
<td>50.9</td>
<td>51.3</td>
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<td>0.93</td>
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<td>Skin</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>44.6</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Femur</td>
<td>-</td>
<td>60 (D_{1cc})</td>
<td>-</td>
<td>43.7</td>
<td>-</td>
<td>-</td>
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</table>

Dose painting distributions and DVHs in FDG PET/CT defined sub-regions

(Serban et al, ASTRO 2012)
PET/CT FOR RADIOTHERAPY TREATMENT PLANNING IN PATIENTS WITH SOFT TISSUE SARCOMAS

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in vivo 23: 105-110 (2009)

11C-Methionine vs. 18F-FDG PET in Soft Tissue Sarcoma Patients Treated with Neoadjuvant Therapy: Preliminary Results

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EJRO 2003; 29: 908-915

Thallium-201 scintigraphy—a predictor of tumour necrosis in soft tissue sarcoma following preoperative radiotherapy?

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Oncologic PET/MRI, Part 2: Bone Tumors, Soft-Tissue Tumors, Melanoma, and Lymphoma

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**18F-FDG PET** does not add information to MRI for T-staging in soft-tissue sarcomas. On the other hand, 18F-FDG PET provides additional prognostic information.

**DW-MRI** has been shown to provide a measure of tumor cellularity and could serve to identify areas for boost dose of radiation as **dose painting**.

**DCE-MRI** could map the areas of neoangiogenesis and serve for **dose painting**.

**MR-spectroscopy** could potentially contribute to differentiation between malignant and benign soft-tissue masses and help in **dose painting** showing hypoxic areas.
Adaptive Radiotherapy?
Group 1: increase in tumor size

Group 2: no change or decrease in tumor size

Similar local control and survival in both groups
Radiation-Induced Inhibition of Tumor Growth as Monitored by PET Using L-[1-\textsuperscript{11}C]Tyrosine and Fluorine-18-Fluorodeoxyglucose

Bernard J. G. Daemen, Philip H. Elsinga, Anne M. J. Paans, Andre R. Wieringa, Antonius W. T. Konings, and Willem Vaalburg

FIGURE 1. Time schedule of the experimental procedure for PET measurements. Carbon-11-tyr (□) and \textsuperscript{18}FDG (■) data were acquired for 45 min. Time interval between \textsuperscript{11}C-Tyr and \textsuperscript{18}FDG studies is 4 hr.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Growth delay (GD)</th>
<th>P value</th>
<th>Number</th>
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<tbody>
<tr>
<td>10 Gy</td>
<td>1.98 ± 0.09</td>
<td>p &lt; 0.004</td>
<td>n = 8</td>
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<tr>
<td>30 Gy</td>
<td>3.54 ± 0.32</td>
<td>p &lt; 0.016</td>
<td>n = 6</td>
</tr>
<tr>
<td>50 Gy</td>
<td>4.47 ± 0.38</td>
<td>p &lt; 0.016</td>
<td>n = 6</td>
</tr>
<tr>
<td>15 min at 45°C</td>
<td>0.17 ± 0.04^*</td>
<td>p &lt; 0.11</td>
<td>n = 6</td>
</tr>
<tr>
<td>30 Gy + 15 min at 45°C</td>
<td>6.75 ± 0.04</td>
<td>p &lt; 0.07</td>
<td>n = 4</td>
</tr>
</tbody>
</table>

Values are mean ± s.e.m.

P values obtained with Fisher's distribution free sign test (25).

MET-PET uptake showed a mean T/N (Tumor/Non-Tumor) ratio of 4.58 ± 2.57. After CIRT, the mean T/N ratio decreased to 3.11 ± 2.04 significantly ($P < 0.00029$).

Advantage compared to FDG-PET:
- early changes
- better prognostic value
Also FLT-PET could be considered
Imaging for Verification of RT
Conclusions

- CT and MRI (especially in the extremities) are the standard imaging modalities to identify and outline the target and non-target structures for radiotherapy planning.

- PET (not only with FDG), DW-MRI and PW-MRI are a very exciting research fields to implement dose painting and biologically adaptive radiotherapy.