Photoacoustic metastases detection using clinically approved SPIO dispersions

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Introduction and Hypothesis

- Patient prognosis and treatment based on accurate nodal staging
- Pre-operative nodal MR staging for different malignancies can be improved using Super Paramagnetic Iron Oxide (SPIO) nanoparticles
- Uptake of SPIOs in healthy nodal tissue compared to absence of uptake in malignant tissue
- Photoacoustically imaging SPIO deposits within nodal tissue could lead to a fast intra- or pre-operative nodal staging technique

Benefit of the approach

- SPIO nanoparticles proven to improve nodal staging using MRI
- Optical properties of SPIOs favorable for PA detection
- Clinical approved SPIO dispersions commercially available
- Availability facilitates rapid clinical applicability

Tomographic photoacoustic setup

- Curvilinear 32 element ultrasound detector array
- Central frequency 6.25 MHz with 80% FBW
- Elevation plane focus of 1 mm with axial resolution of 150 µm
- Repetition rate: 10 Hz - Pulse duration: 10 ns
- Projections: 20 (18 degree) - Energy: 20 mJ/cm² at 720 nm
- Averages: 100 - Slice acquisition time: 200 seconds

Results

- Nodal tissue shows no PA response without contrast injection
- SPIO deposits within nodes possible to map using PA tomography
- Distribution of SPIOs comparable with results of 14 T MRI and histology
- SPIO deposition mostly in the periphery of the node

<table>
<thead>
<tr>
<th>Number lymph node</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iron amount (µg)</td>
<td>27±2</td>
<td>51±4</td>
<td>40±3</td>
<td>49±3</td>
<td>30±2</td>
<td>11±1</td>
</tr>
<tr>
<td>Absorption coefficient (\bar{\mu}_a) (mm⁻¹)</td>
<td>0.14±0.01</td>
<td>0.27±0.02</td>
<td>0.21±0.02</td>
<td>0.26±0.02</td>
<td>0.15±0.01</td>
<td>0.06±0.01</td>
</tr>
</tbody>
</table>

Measured amount of iron within each node (µg) and corresponding \(\bar{\mu}_a\) (mm⁻¹) estimated using physical properties of the SPIO and Mie scattering simulations.

Experimental animal model

- Evaluation in healthy rat model
- Subcutaneous injection of 0.1 ml Endorem® in dorsal side hindleg
- After 24 hours resection of the node
- Photoacoustic and 14 Tesla MR imaging of the resected lymph nodes
- Additional verification of SPIO distribution and quantity using H&E staining and Vibrating Sample Magnetometry

Outlook

- PA detection of SPIOs creates possibilities for intra-operative nodal assessment in oncology
- Evaluation of concept inside a metastatic animal model in progress
- Rapid implementation into the clinic due to the availability of clinically approved dispersions
- Towards compact intra-operative imaging modality for resected lymph node assessment

Top: Comparison in measured SPIO distribution between PA and 14 Tesla MR imaging. SPIOs mainly distributed in the periphery of the nodal volume (white dotted line).

Bottom: Node with and without SPIOs after paraffin embedding and H&E staining.

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