SpinoTemplate: A System for MR-Guided Spinal Cellular Therapeutics Injections

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Target audience: Scientists and clinicians interested in MR-guided therapeutics Injections into the spinal cord.

Purpose: Patients with Amyotrophic Lateral Sclerosis (ALS), also known as Lou Gehrig's disease, have limited treatment options [1]. Small animal models have shown promise for halting the neurodegeneration associated with ALS when cellular therapeutics are delivered to the ventral horn of the spinal cord [1-3]. The operation currently utilized to deliver cells to the cord involves an invasive surgery requiring multi-level laminectomy and dissection of the dura mater. Our goal was to develop a template-based needle guidance system, *SpinoTemplate* (Fig.1b), to deliver stem cells percutaneously under MRI guidance with the aim of improving upon the existing invasive and time-consuming surgical techniques for targeting injection sites for cell infusion.

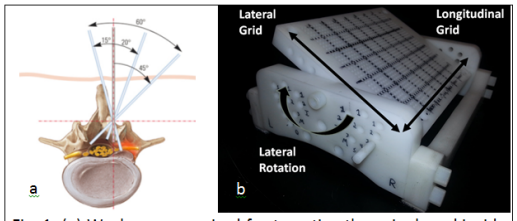

Fig. 1. (a) Workspace required for targeting the spinal cord inside intact vertebrae. (b) SpinoTemplate, showing the template (angled), support structure and the three targeting axes

Methods: The device had specific design criteria, including: 1.5/3T MRI-compatibility, needle insertions must be performed manually by the surgeon, the ability to guide the needle through gaps between vertebrae (Fig.1a), the ability to target multiple points along the spine without adjusting the mounting system, minimally invasive mounting of the device on the patient, and ensuring the device was disposable in its final iteration. These requirements are met by employing a plastic, low-cost, rotating 10x10cm needle targeting template mounted via a tight-fitting neoprene wrap and sutures joining the skin and support frame (Fig1b). After mounting the template on the phantoms/specimens in a 3T Siemens Trio MRI scanner, the following steps were taken:

- An MR surface coil was placed over the template and subject.
- High-resolution images containing the spinal targets and five gadolinium spherical fiducial markers (Beekley Inc.) embedded in the template were made using a 3-D T1-weighted (T1w) fast gradient echo sequence (MP RAGE). Tissue targets at the spinal cord were identified in MR images.
- Images were loaded into the template targeting software. Registration was performed between the MRI and the template frames of reference. A needle trajectory that reaches the tissue target was determined, giving positional information of the template angle, lateral and longitudinal hole position, and needle insertion depth.
- A 16 gauge rigid outer cannula with a rigid central stylet was advanced manually. The stylet was removed and an inner 26 gauge cannula was inserted through the needle guide. The template allowed the needle to be advanced to the target position in the spine.
- Saline-diluted gadolinium contrast agent (1% Gd) was injected through the needle to visualize the injection site. After injection, the needle was extracted and a T2*-weighted gradient echo sequence confirms location and delivery of the gadolinium. This step can be replaced with MRI-labeled cellular therapeutics.

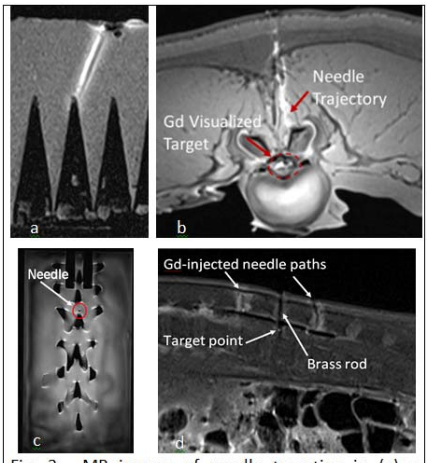

Fig. 2. MR images of needle targeting in (a) a geometrical phantom, (b) an ex-vivo mature swine (transverse), (c) a human spine phantom (coronal), and (d) in an ex-vivo piglet (sagittal). Needle trajectories and targets were visualized with gadolinium in (a-b,d) and a brass rod in (c-d)

Preliminary tests to validate the accuracy of the template were carried out using a geometric phantom (n=30), a glass container containing 3D-printed plastic pyramids embedded in an agar gel (Fig.2a). Gadolinium contrast agent was used for trajectory and target visualization. Axial and radial errors of the needle were calculated based on the distance between the visualized trajectory and the tip of the target pyramid. Further tests for system feasibility were performed in human spine phantoms (n=3), ex-vivo mature swine spines (n=5) and euthanized piglets (n=3) (Fig.2b-d).

Results: The MSE of the registration between fiducial markers in the template and MRI scanner coordinate systems was <0.5mm per marker. The template coordinate system handled the subsequent targeting calculations. Phantom tests showed a targeting accuracy (means-squared error, MSE) of 2.1 mm (Fig.3a). Fig. 3b-c indicates the targeting error distribution in the radial and axial directions of the needle. Preliminary results showed successful MRI-guided injections in spine phantoms, ex-vivo swine spines and euthanized piglets. The needle was successfully guided between the vertebrae into the spinal cord. The procedure time is approximately 35 minutes including template setup, template-scanner registration, target localization, trajectory planning, needle injections and confirmation scans. An additional 5 minutes was required per additional injection during a procedure.

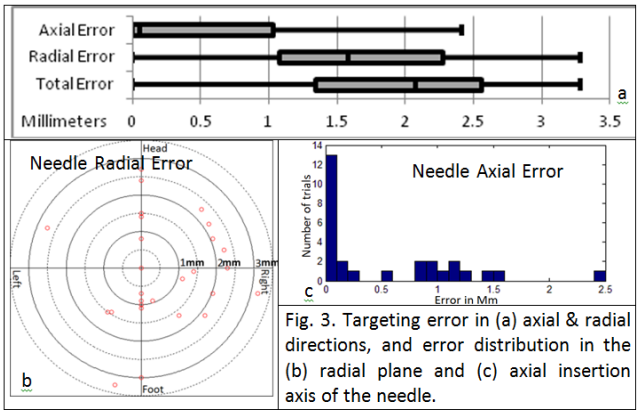

Fig. 3. Targeting error in (a) axial & radial directions, and error distribution in the (b) radial plane and (c) axial insertion axis of the needle.

Conclusion: SpinoTemplate for MRI-guided percutaneous spinal procedures has been evaluated on phantom models, ex-vivo mature swine spines, and euthanized piglets, showing accurate spinal targeting with possible use in spinal cellular therapeutic injections under 3T MRI guidance.

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References: [1] M. Asheuer et al., PNAS, 2004;101(10):3557-3562. [2] J. Goolsby et al., PNAS, 2003;100(25):14926-14931. [3] M. Hoehn et al., PNAS, 2002; 99(25):16267-16272.