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MR-guided stereotactic navigation

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ABSTRACT

Functional magnetic resonance imaging allows precise localization of brain regions specialized for different perceptual and higher cognitive functions. However, targeting these deep brain structures for electrophysiology still remains a challenging task. Here, we propose a novel framework for MRI-stereotactic registration and chamber placement for precise electrode guidance to recording sites defined in MRI space. The proposed "floating frame" approach can be used without usage of ear bars, greatly reducing pain and discomfort common in standard stereotactic surgeries. Custom pre-surgery planning software was developed to automatically solve the registration problem and report the set of parameters needed to position a stereotactic manipulator to reach a recording site along arbitrary, non-vertical trajectories. Furthermore, the software can automatically identify blood vessels and assist in finding safe trajectories to targets. Our approach was validated by targeting different regions in macaque monkeys and rats. We expect that our method will facilitate recording in new brain areas and provide a valuable tool for electrophysiologists.

1. Introduction

Neural recordings have been traditionally guided by atlas based stereotactic planning. However, most atlases are based on a single animal (Paxinos et al., 2000; Saleem and Logothetis, 2007; Paxinos and Watson, 2007), which introduces the problem of intersubject variability. Furthermore, precise localization and alignment of internal features, such as Bregma and Lambda, on the same plane can be very challenging due to variability in suture appearance. Any deviation from the Bregma-Lambda or Ear Bar Zero (EBZ) plane will introduce significant deviations in deep brain targeting. Another associated problem with atlas based targeting is the risk of hitting a blood vessel. Many region of interests (ROIs) are located directly below major blood vessels, ruling out vertical penetration due to the risk of intracerebral hemorrhage.

With the increased availability of functional localizers it is now possible to pinpoint, with exquisite sub-millimeter precision, brain regions representing visual, auditory, somatosensory information or those participating in higher cognitive functions, such as decision-making and language (Sereno et al., 1995; Kayser et al., 2007; Moeller et al., 2008; Tootell et al., 1995; Tsao et al., 2003). While fMRI can report activity on a global scale, its temporal and spatial characteristics cannot replace data obtain with electrophysiology, and fMRI activity is only an indirect reflection of underlying activity (Logothetis, 2008; Sirotin and Das, 2009). Thus, electrophysiological characterization of neural activity in fMRI-identified brain regions is critically needed.

Targeting structures which have been identified in MRI for electrophysiological recording is challenging due to the inherent difference in coordinate systems. While a specific region of interest can be easily and precisely defined in MR space in voxel coordinates, recordings are guided according to stereotactic coordinates. The problem, therefore, is to find a way to register these two systems and to translate a given position and orientation in MR space to a set of parameters that configure the stereotactic arm manipulator to target the intended ROI (Fig. 1).

A traditional solution to the registration problem is to identify in the MR scan a set of features that can be used to determine how the brain would be oriented once the animal is positioned in the stereotactic frame (Paxinos et al., 2000; Saleem and Logothetis, 2007). Physically, stereotactic coordinates are defined by the line passing through the ear canals (AP0) and the horizontal plane passing through the interaural line and the infraorbital ridge. These skeletal features, however, are difficult to localize precisely in anatomical scans: (1) The ear canals are especially vulnerable to magnetic susceptibility artifacts, which can cause spatial mislocalization of the interaural line. (2) The eye orbitals are impossible to see with standard anatomical sequences, leading to use of alignment of the anterior and posterior commissures as an alternate definition of the

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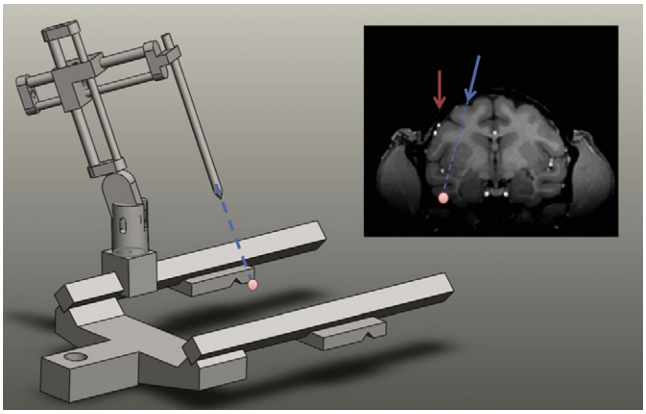

Fig. 1. The general targeting problem. A target in an MR scan (pink dot) is selected according to anatomical or functional considerations. The problem is to position the stereotactic manipulator such that the tip aligns with the desired trajectory. Notice that blood vessels above the target site (small white dots) pose a problem for simple vertical penetration (red line), while a non-vertical trajectory can safely reach the target (blue line). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

horizontal plane. Significant mismatch can occur between this definition and the physical definition, leading to a large error during actual stereotactic surgeries.

Here, we propose a novel framework that solves the general registration problem between the MR coordinate frame and the stereotactic frame during the surgical procedure (Fig. 2). The method relies on a machine vision algorithm that finds the optimal transformation between the two coordinate frames by registering a small number of artificial external markers. The framework allows positioning a recording chamber, according to pre-surgery planning, and is not limited to vertical penetrations. Since the registration problem is solved in real time, the stereotactic frame can be physically detached from the animal (ear bars are not inserted to the ear canals). This “floating frame” approach permits implantation of chambers while the animal is simply head fixed in the primate chair, greatly reducing discomfort and complications involved in full stereotactic surgery.

We designed general purpose pre-surgery planning software that can be used with various stereotactic frames and manipulators (available for download from http://www.tsaolab.caltech.edu/) and hence is of usage not only for primate research, but also for smaller animals. The software enables visualization of anatomical and functional scans and allows the user to position virtual chambers, cannulae, grids and electrodes that can assist in precise planning of electrodes’ trajectories. The software greatly assists in targeting recording sites by automatically scanning the search space of grid parameters (rotation, tilt angle, hole in grid) and reporting optimal parameters that minimize the distance to a predefined target.

Another novel feature of our software is the ability to automatically identify blood vessels in MR scans and to suggest safe chamber placements and electrode trajectories which avoid passing through them. Such solutions typically require the usage of all degrees of freedom of the stereotactic manipulator. To obtain the values required to position the stereotactic manipulator in such a way we model the stereotactic manipulator as a robotic arm and use an inverse kinematic algorithm to recover the exact parameters needed (Fig. 2). This approach is generic and the system can solve the problem for any stereotactic manipulator, as long as the user can supply a 3D description of its joints.

We envision that this system will be a valuable tool for electrophysiologists and will facilitate recordings in new brain areas, as well as other types of experiments requiring precise stereotactic targeting, e.g., injection of viral vectors or pharmacological compounds to MR-defined targets. Here, we provide experimental validation from monkeys and rats, as well as computer simulations that give the expected chamber placement error in terms of positional and angular uncertainties.

2. Methods

2.1. Animals and surgery

Three male rhesus macaques, weighing 6–8 kg were used in the experiments. Surgical procedures followed standard anesthetic, aseptic, and postoperative treatment protocols. The head-post was implanted in two surgical procedures separated by several weeks recovery time. First, the monkey was anesthetized

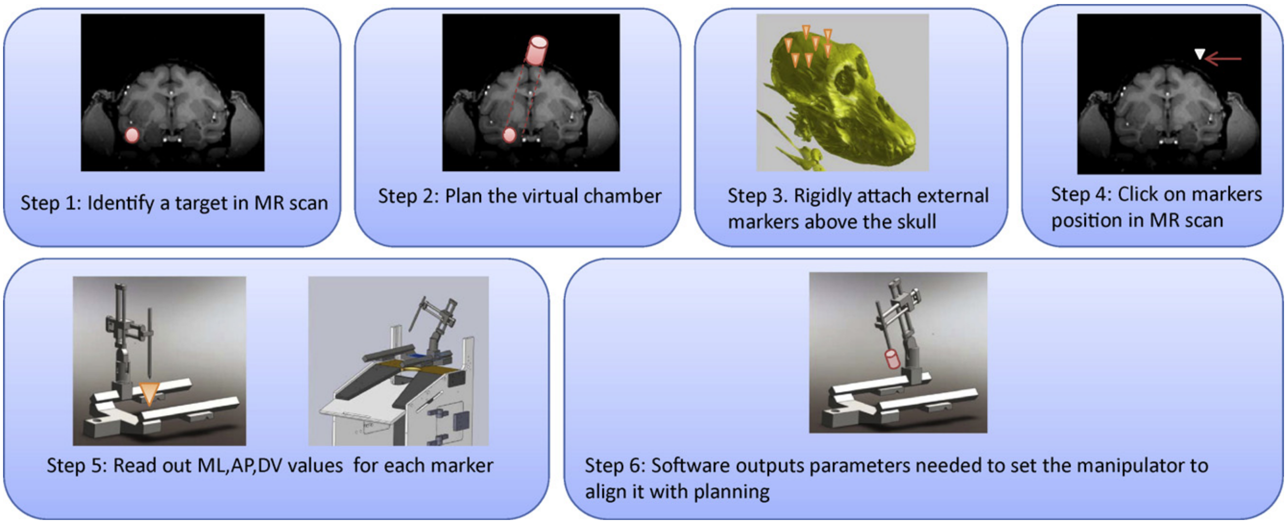

Fig. 2. Framework overview. A brain region is selected for targeting and a virtual chamber is placed. Several external markers are rigidly attached to the skull by drilling into an existing implant or securing a small attachment to the head post (not shown). Marker positions in the MR image is identified. During the surgical procedure the position of the markers is read out using the stereotactic manipulator. This can be done even if the stereotactic frame is not physically attached to the animal, but instead to the primate chair. The software solves the targeting problem given the read out values and outputs the set of parameters that are needed to align the manipulator with the planned virtual chamber position. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)