Combined Magnetic-Resonance and Bioluminescence Imaging of Live Mice

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Introduction

Three-dimensional Bioluminescence imaging (BLI) is a valuable tool to visualize, track and understand biological processes in living animals. Utilizing internal light sources, such as luciferase, BLI measures an intensity map on the animal's skin for the light produced. Although this gives an approximate location of the light source, it does not give precise information about the anatomical location and does not provide quantitative information. Magnetic resonance imaging (MRI) provides three-dimensional high-resolution anatomy. Therefore, co-registering BLI with MRI images is essential to enable this molecular imaging technique to be exploited to the fullest extent. This abstract describes a platform and specialized MR coil to enable BLI and MRI with identical posture.

Methods

Three female CD1-Nude mice (Charles River Labs, Wilmington, MA), aged from 3 to 9 months were surgically implanted with tritium-filled glass vessels (MB-Microtec, Bern, Switzerland, 0.9 mm diameter, 2.5 mm length) to simulate bioluminescent sources.

To enable sequential MR and BL imaging without disturbing the animal posture, a custom MR-compatible platform was designed and fabricated to be used in both instruments (Figure 1). The platform allows a mouse with stretched limbs to be supported on a fine nylon filament net which is preferable for bioluminescence imaging. For MRI, the platform was integrated in a larger setup that is comprised of three parts; the radio frequency (RF) coil, the supporting base, and the platform itself. To maximize the signal-to-noise ratio (SNR) in the MR images, a 5 cm diameter, 15 cm long modified high-pass birdcage coil was built to closely fit the outstretched mouse. Since the platform was 8.5 cm wide, the coil was split into two asymmetric parts (above and below the platform) that were inductively coupled. The capacitors in the coil end-rings were individually selected to balance the currents in the rungs.

The supporting base incorporates the lower portion of the RF coil and positions the platform at the center of the gradient coil of the MRI. Physiological monitoring sensors for ECG, respiration and cutaneous temperature were embedded on the top surface to contact the mouse through the nylon filament net when positioned on the platform. A custom closed-looped warm air heating system (not shown) was also supported by the base to keep the mouse warm throughout the experiment.

The magnetic resonance imaging were performed with a 7-Telsa Inova scanner from Varian Inc. (Palo Alto, CA, USA) using a 3D fast spin-echo sequence with a field of view to cover the entire mouse [TE = 7.1 ms (effective), TR = 300ms (two heartbeats), isotropic resolution = 0.208 mm, FOV 25 x 37 x 100 mm^3, 6 echoes, 4 averages]. The mouse was maintained under Isoflurane and prospectively gated to the ECG and respiration during the 120 min scan.

The bioluminescence imaging was performed immediately following the MRI imaging using an IVIS-3D prototype system from Xenogen (Alameda, CA, USA). Of the three parts used for the MRI scan, only the platform was used in the BLI scan. The RF coil was carefully removed and the platform was transferred to the BLI while the mouse remained in the same posture under Isoflurane anesthesia. The luminescence images were acquired in 8 views (45 degrees apart), at 3 different wavelengths (580, 620 and 640 nm) for 3 min each.

The MRI and BLI images were first manually aligned using the 3D visualization software AMIRA (Mercury Computer Systems, San Diego, CA, USA).

To remove any residual differences, the two images were registered automatically using a non-linear transformation program called MINCTRACC, distributed by the Montreal Neurological Institute of McGill University[1,2].

Results

The magnetic-resonance images and bioluminescence images were acquired under the same conditions for all three mice.

The MRI images were registered in two steps to the surfaces created from the luminescence imaging software (Figure 2). After the manual linear registration, the contours of the MRI and BLI images were at most 2.8 mm from each other. The largest discrepancy was found where the mouse was resting on the raised pneumatic respiration sensor during the MRI imaging; this pad was absent during the BLI imaging. The second automatic non-linear registration step successfully aligned the position of the skin in the two images to within 0.4 mm (2 voxels) of each other.

References

[1] Collins *et al*. Journal of Computer Assisted Tomography, 8(2):192–205, 1994.
[2] Collins *et al*. Human Brain Mapping, 3:190–208, 1995.

Figure 1. Exploded computer drawing of the platform on which the MRI and BLI imaging were performed.

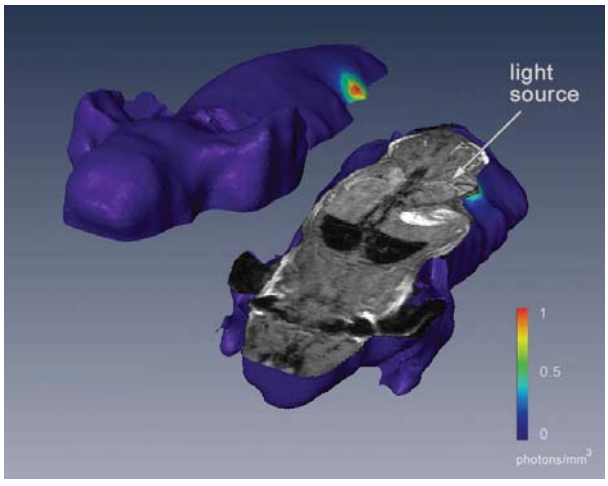

Figure 2. Combined BLI and MRI image. The luminescence scale was normalized to the peak intensity.