Correlating in vivo MRI with 3D post mortem information in rat brain

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Problem: In the context of validating novel MR contrast agents or PET / SPECT tracers, one is often faced with the problem of correlating in-vivo 3D data (MR, SPECT or PET) with ground-truth derived from post-mortem 2D information (photographic imaging, histological stains, autoradiography, etc.). With increasing efforts being geared towards accurate quantitative measures, the typical manual fitting of post-mortem 2D slices to in-vivo 3D volumes suffers from lack of repeatability and limited accuracy. In an effort to control these variables that play an important part in the final quantification of agent characteristics, we developed a number of tools enabling the automatic reconstruction of 3D volumes from post-mortem data [1], and the automatic registration of these volumes to their in-vivo correspondent. We present here our latest work in the latter, in particular our first results of automatic deformable registration of photographic post-mortem volumes to in-vivo MR data (MRI 7T).

Methods: The core theoretical aspect of our registration method can be formulated as follows: given two images I (source) and J (target), registration can be formulated as maximizing the likelihood of the transformation relating both images which, under quite general assumptions [2], boils down to $L(T) = \sum_k \gamma(I_k, J_{T(k)})$ where $\gamma(i,j) \equiv \log\left(p(i,j)/p(i)p(j)\right)$, $I_k = I(k)$, and $p(i,j), p(i), p(j)$ correspond to the joint intensity and marginal pdfs of I and J, respectively. This formulation closely relates with the concept of empirical mutual information advocated in [3]. In the deformable registration case, we are estimating local deformations such that $T_k = T_k^a + u_k = T_k^a + \sum_m a_m G(k - c_m)$, where T^a is the affine component of the transformation, u_k is the deformable component, modelled by Gaussian radial basis functions (RBF) $G(x) = \exp(-\beta\|x\|^2)$, a_m are the RBF coefficients, and c_m are the RBF control point locations. In order to maximize the similarity measure $L(T)$, we use a gradient descent method [4] which requires the derivatives of the criterion L with respect to the transformation parameters a_m. For the sake of simplicity, we will assume here that the affine component of the transformation is held fixed. In practice, it can be optimized separately from the deformation parameters, leading to an alternate optimization scheme. The derivative of our measure is then $\partial L/\partial a_m = \sum_k \left(\partial L/\partial u_k \times \partial u_k/\partial a_m\right)$. It can be shown [5] that $\partial L/\partial u_k = f_k = \left(G * \partial\gamma/\partial j\right)(I_k, J_{T(k)})\nabla J_{T(k)}$ where $\partial\gamma/\partial j = \partial\hat{p}/\partial j/\hat{p} - \partial\hat{p}_j/\partial j/\hat{p}_j$ and that $\partial u_k/\partial a_m = G(k - c_m)$. Our gradient descent algorithm thus yields the iteration $a_m^{(n+1)} = a_m^{(n)} + \alpha^{(n)} \sum_k f_k G(k - c_m)$, where $\alpha^{(n)}$ is chosen such that $\max_k \sum_m f_k G(k - c_m)$ is half a voxel spacing.

In practice, two important aspects are essential for our approach to work. First, rigid registration was performed using a standard registration method [2]. This type of initialization is typical of any deformable registration method and most optimization strategies; the closer the initial transformation is to the optimal one, the higher the chance of a successful registration. Second, a pyramid approach was used where the technique described above was applied at each level of the pyramid. Again, these types of pyramid strategies are often encountered in registration techniques and greatly improve the convergence characteristics.

Results: Figure 1 shows the result of deformable registration**.** The image on the left show the contours of a photographic volume of a rat brain (200x140x150 voxels, 0.1x0.1x0.1 mm^3) overlaid on the corresponding MR image (256x256x57 voxels, 0.2x0.2x0.5 mm^3 resolution) after rigid registration (note the brain surface misalignment). The next image shows the same contours after deformable registration, where the brain surface is much better aligned. To appreciate the effect of deformations on the photographic volume, the next two images display the deformed photographic volume by itself, and overlaid on the MR image.

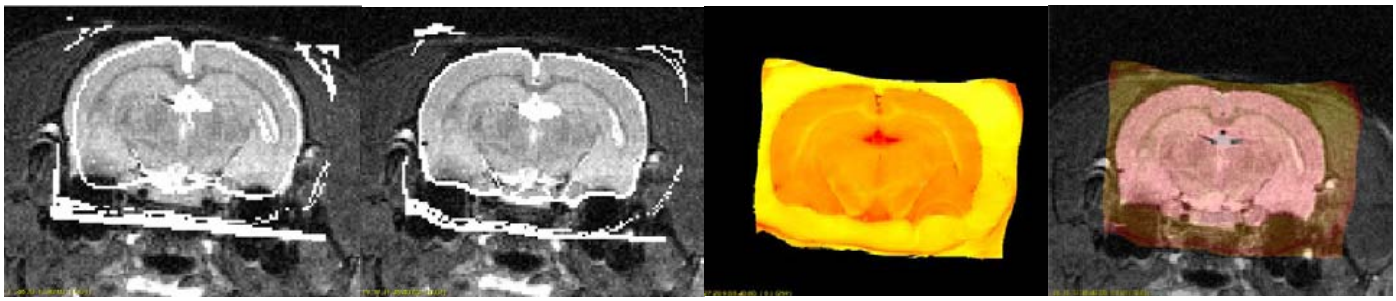

Figure 1 From left to right: 1) Photograph contours (white) overlaid on MRI after rigid registration, 2) after deformable registration, 3) Photograph after deformable registration, 4) Photograph overlaid on MR image.

Conclusion: We have presented our deformable registration strategy to match photographic data to in-vivo images in an effort to gain control over measure misalignments between in-vivo and post-mortem data in the context of tracer validation. We believe such methods may play a central role when quantification of contrast agent / tracer characteristics becomes important because 1) 3D-3D registration will be more accurate than 2D-3D registration due to the greater amount of information exploitable during the registration process, and 2) the subsequent analysis can be made in 3D thus enabling measurements on complete structures instead of slices. A larger study performed on a large set of images from several rats is currently examining the accuracy and robustness of this method in this context and its effect on quantification.

References:

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