Unbiased Diffeomorphic Shape and Intensity Atlas Creation: Application to Canine Brain

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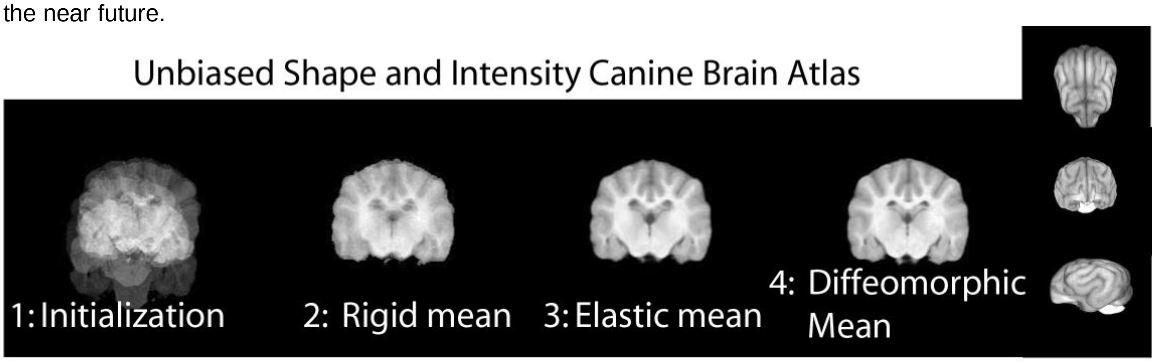
Introduction: High dimensional deformable image registration [1] is important for spatially locating functional activation [2], understanding disease progress [3] and for improving the statistical power of clinical trials [3]. The coordinate system chosen for a particular structural or functional study influences the quantitative outcome, as the reference frame affects the measurement in the nonlinear world of morphometry [4]. The statistically conservative approach thus requires *least biased* coordinate systems where average anatomical configurations are estimated from a spatially normalized population [1,4,5]. Prior work on this problem falls into two categories: deformation-based averaging [1] and intensity-based averaging [5]. The advantage of intensity averaging is that it removes dependence on the intensity signature of any single, specific anatomy. Intensity averaging may create false structures by averaging tissues that are not in correspondence [5]. Another disadvantage is that the residual of the geometric (or shape) component of the average may be far from zero. Shape-based averaging, on the other hand, guarantees that tissues are in correspondence before averaging and gives a minimal shape residual. However, initialization is with respect to a specific anatomical space [1], inducing a dependence on the initial anatomy. This paper outlines a procedure that uses intensity averaging to gain an unbiased initialization for shape-based averaging, giving a best-of-both-worlds result. The method, here, provides an average dog brain atlas. The atlas defines a common canine-stereotactic space used to interpret patterns of cortical activation to visual stimuli and for identifying primary and extrastriate cortical areas.

Materials: Each dog image is the average of two, 15-minute MPRAGE images acquired at 3T on a Siemens Trio using a USA head coil. Each animal was sedated, paralyzed and ventilated during image acquisition. Each dog cerebrum was segmented from the cranial cavity using semi-automated open-source methods available in ITK SNAP (www.cognitica.com/snap). The algorithms discussed below are also implemented in ITK.

Methods: We used a cascade of transformations to generate an unbiased shape and intensity atlas. Figure 1 illustrates the process. After skull stripping, the initial distribution of brains was estimated by directly averaging intensities. The second step involved rigidly registering each image to the intensity distribution using ITK mutual information as a similarity metric. We then used a trimmed average [5] of the rigidly registered intensities to gain a much tighter distribution. The next stage uses an elastic registration model to find a sharper trimmed average intensity image and a small deformation shape average. The final step uses large deformation diffeomorphic image registration and shape averaging to bring all structures into exact correspondence, yielding the final unbiased intensity average and the final optimal shape anatomy. The critical step in computing the optimal shape is solving an *average transport* ordinary differential equation forward in time, as described in [1].

Results and Discussion: A three-dimensional rendering of the average shape and intensity dog brain is at right in Figure 1. The final estimate to the average anatomy satisfies two important properties: (1) the image appearance is independent of any specific anatomy; (2) the image shape is independent of any individual's anatomical coordinate system. This result improves upon previous work by guaranteeing *both* of these properties. These properties implicitly assume that the structural correspondences are correct. Given the relative consistency of canine cortical anatomy, we believe that the automated image registration methods (non-landmarked) are adequate. We intend to evaluate landmarked approaches to large deformation shape averaging on human datasets in the near future.



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