Semiautomated Motion Correction of Tumors in Lung CT-perfusion Studies

Adam Chandler, PhD, Wei Wei, MS, Delise H. Herron, BS, RT, Ella F. Anderson, RT, Valen E. Johnson, PhD, Chaan S. Ng, MD

Rationale and Objectives: To compare the relative performance of one-dimensional (1D) manual, rigid-translational, and nonrigid registration techniques to correct misalignment of lung tumor anatomy acquired from computed tomography perfusion (CTp) datasets.

Materials and Methods: Twenty-five datasets in patients with lung tumors who had undergone a CTp protocol were evaluated. Each dataset consisted of one reference CT image from an initial cine slab and six subsequent breathhold helical volumes (16-row multi-detector CT), acquired during intravenous contrast administration. Each helical volume was registered to the reference image using two semiautomated intensity-based registration methods (rigid-translational and nonrigid), and 1D manual registration (the only registration method available in the relevant application software). The performance of each technique to align tumor regions was assessed quantitatively (percent overlap and distance of center of mass), and by a visual validation study (using a 5-point scale). The registration methods were statistically compared using linear mixed and ordinal probit regression models.

Results: Quantitatively, tumor alignment with the nonrigid method compared to rigid-translation was borderline significant, which in turn was significantly better than the 1D manual method: average (± SD) percent overlap, 91.8 ± 2.3%, 87.7 ± 5.5%, and 77.6 ± 5.9%, respectively; and average (± SD) DCOM, 0.41 ± 0.16 mm, 1.08 ± 1.13 mm, and 2.99 ± 2.93 mm, respectively (all $P < .0001$). Visual validation confirmed these findings.

Conclusion: Semiautomated registration methods achieved superior alignment of lung tumors compared to the 1D manual method. This will hopefully translate into more reliable CTp analyses.

Key Words: CT perfusion; image registration; lung tumor.

Image registration and motion correction are generic problems which impact on many areas of imaging and radiology. One specific area in which they may have a potential impact is in computed tomography perfusion (CTp).

There is increasing interest in the ability of CT to evaluate perfusion of tumors to better understand the effects of treatments and therapies on tumors (1). CTp is an evolving technique with potentially wide-ranging applications in oncology, including diagnosis, treatment evaluation, and prognostication (2). The technique relies on the acquisition of time-intensity plots from tissues of interest and vascular supply after intravenous administration of a tracer (iodinated CT contrast medium). Tissue perfusion parameters can then be derived from this information and the application of physiological modeling (3). Parameters that can be derived include tissue blood flow, blood volume, and permeability surface area product.

CTp requires acquisition of the time-intensity data for a sufficient length of time to adequately characterize the perfusion of tissues. To maintain spatial fidelity, it also requires the data be obtained from pixels that are fixed in space. Imaging protocols have been developed to meet these requirements by acquiring multiple images (at the same spatial location) in an axial cine mode during uptake and washout of an injected contrast bolus through the tissues. Such imaging protocols are sufficient for relatively stationary organs and tissues, such as those in the brain (4,5) and pelvic cavity (6), but can be severely compromised when imaging organs and tissues where breathing motion occurs, such as the lung. One technique that has been adopted to limit the misregistrations because of breathing for lung CTp imaging is to obtain the cine data during breathhold conditions. The particular challenge for lung CTp is that data acquisition typically needs to extend beyond 30 seconds, which is a practical limit for a single breathhold in many patients. One solution is to subsequently acquire a series of sequential helical CT volumes (each acquired under breathhold conditions) for a period of between 1 and 2 minutes after the initial acquisition of cine

Acad Radiol 2011; 18:286–293

From the Departments of Imaging Physics (A.C.), Biostatistics (W.W., V.E.J.), Diagnostic Imaging (D.H.H., E.F.A.), and Radiology (C.S.N.), MD Anderson Cancer Center, 1400 Pressler Street, Houston, TX 77030; Advanced Applications Engineering Team, GE Healthcare, Waukesha, WI (A.C.). Received September 9, 2010; accepted October 20, 2010. **Address correspondence to:** C.S.N. e-mail: cng@mdanderson.org

doi:10.1016/j.acra.2010.10.008

mode data. Such data could inherently cause misregistration relative to the cine mode data because of the images being acquired during different breathhold conditions and over different image extents.

The motivation for this work was that, unfortunately, the particular CTp software package being used in our work, CT Perfusion 4 (GE Healthcare, Waukesha, WI), currently has no specific software/functionality to compensate for tumor misregistrations that may occur in lung CTp protocols between the helical and axial cine images. The only method currently available to us in this application is manual selection of images from the helical volumes (a one-dimensional [1D] manual registration) (ie, hand picking images that anatomically match the cine images on visual inspection). This is clearly extremely time-consuming, and furthermore is prone to errors. Availability of an automated or semiautomated registration algorithm would be advantageous; however, clearly, it is a prerequisite that the methodology be validated before incorporation into CTp analyses.

Intensity-based registration algorithms that use information-based similarity measures have been used for a variety of medical image registration applications (7). Such algorithms assume that the two images to be registered have high levels of corresponding image information and therefore lend themselves well to three-dimensional (3D)-3D registration tasks. There is, however, a subset of registration applications in which the images to be registered only partially match in image extent and corresponding image information (8). The lung CTp registration task addressed in this work falls into this latter group and is potentially a more challenging registration task for intensity-based registration algorithms (cine mode data has limited z-axis coverage, of the order of 2 to 4 cm, whereas helical data has much more extensive coverage).

In this work, we investigate the accuracy of rigid-translational and nonrigid intensity-based registration techniques to recover tumor misregistration in data acquired from lung CTp datasets, as well as comparing the results to those obtained from the currently available 1D manual registration method.

MATERIALS AND METHODS

Data for this study were obtained from a prospective institutional review board approved CT perfusion study in which 12 patients with lung tumors had been enrolled. The tumors were primary or secondary malignancies on clinical or pathological evaluation. The mean age of patients was 54.4 years (range, 21-74 years; 7 male, 5 female). Twenty-five datasets were available for analysis: 11 patients underwent the imaging protocol described in the following section on two occasions and one patient on three occasions.

CT Scanning Technique

CT scans were obtained on a 16-row multidetector CT (LightSpeed, GE Healthcare), with patients in the supine position. Target lesions within the thorax, greater than 3 cm in the minimal axial diameter, were selected by a single radiologist. Scans were obtained in two phases.

Phase 1 (0-30 seconds): low-dose axial cine CT scans over the target lesion (cine mode, 4 x 5mm row detector, 1-second rotation speed, at 120 kVp, 90 mA) were acquired, during a single expiratory breathhold of 30 seconds. CT acquisition commenced 5 seconds after the start of intravenous injection (40 mL nonionic contrast medium [320 mg iodine/100 mL, ioversol [Optiray, Covidien, Hazelwood, MD]), at 7 mL/s, via a power pump injector). The data were reconstructed to 59 cine images (512×512 pixels, 4 slices, 0.7×0.7 mm^2 in-plane pixel size by 5-mm slice spacing, 0.5 seconds temporal resolution).

Phase 2 (50-125 seconds): Six sequential low-dose helical CT scans covering 9.5 cm in the z-axis centered on the index lesion (10-mm collimation, 1.0-second rotation speed, table speed 13.75 mm per rotation, at 120 kVp, 90 mA), at sequential expiratory breathholds, each of approximately 5 seconds, and at 15-second intervals (ie, at 50, 65, 80, 95, 110, and 125 seconds after commencement of contrast medium injection). Each helical volume was reconstructed: a) in-plane to 512×512 pixels of size 0.7×0.7 mm^2; and b) slice spacing of 2.5mm (39 slices total, n = 15), 1mm (96 slices total, n = 3), and 0.5 mm (191 slices total, n = 7).

Image Alignment

The overall goal of image alignment was to select/register a single image from each of the 6 helical volumes (ie, from Phase 2) that aligned with a given reference image from the cine acquisition (ie, from Phase 1), from each dataset obtained. The latter was selected as one of the 59 images in Phase 1 that was not degraded by motion.

Three alignment methods were compared: 1D manual, rigid-translational, and nonrigid. The latter two being semiautomated intensity-based registration methods. Because registration of the tumor was the primary interest in this work, alignment was based on correspondence of tumor anatomy, and not the whole axial CT section.

1D manual alignment. Two observers in consensus viewed the helical volumes of each dataset on a slice-by-slice basis and selected four contiguous slices (ie, 20-mm z-axis volume) from each of the six helical volumes that most closely matched those of the four contiguous reference cine images (abbreviated as HVman). This was undertaken on a workstation (Advantage Windows 4.2, GE Healthcare). This manual alignment methodology essentially equates to a 1D registration (a translation in the z-direction). This is the only practical way that a user can use the CT workstation software for registration of body perfusion data.

Rigid-translational registration. For both semiautomated intensity-based registration methods, the cine reference image was set as the target (or "reference") image and the helical volumes were set as the source (or "floating") images. The