Quantitative Assessment of Effects of Motion Compensation for Liver and Lung Tumors in CT Perfusion

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Rationale and Objectives: To study the effects of four different rigid alignment approaches on both time-concentration curves (TCCs) and perfusion maps in computed tomography perfusion (CTp) studies of liver and lung tumors.

Materials and Methods: Eleven data sets in patients who were subjected to axial CTp after contrast agent administration were assessed. Each data set consists of four different sequences, according to the different rigid alignment configurations considered to compute blood flow perfusion maps: no alignment, translational, craniocaudal, and three dimensional (3D). The color maps were built on TCCs according to the maximum slope method. The effects of motion correction procedures on the reliability of TCCs and perfusion maps were assessed both quantitatively and visually.

Results: TCCs built after 3D alignments show the best indices as well as producing the most reliable maps. We show examinations in which the translational alignment only yields more accurate TCCs, but less reliable perfusion maps, than those achieved with no alignment. Furthermore, we show color maps with two different perfusion patterns, both considered reliable by radiologists, achieved with different motion correction approaches.

Conclusions: The quantitative index we conceived allows relating quality of 3D alignment and *reliability* of perfusion maps. A better alignment does not necessarily yield more reliable perfusion values: color maps resulting from either alignment procedure must be critically assessed by radiologists. This achievement will hopefully represent a step forward for the clinical use of CTp studies for staging, prognosis, and monitoring values of therapeutic regimens.

Key Words: TCC; perfusion imaging; motion compensation; liver; lung; image processing.

Computed tomography perfusion (CTp) represents an important and promising imaging technique for the characterization and monitoring of various tumors at their different stages, since it can provide functional parameters at a high morphological resolution (1). This non-invasive and widely available technique is based on the estimation of the tissue's contrast agent delivery and, accordingly, corresponding hemodynamic parameters, by analyzing time–concentration curves (TCCs), to detect changes in the vascular structure of the tissue, with potential correlation to anomalous blood supply patterns (eg, tumor angiogenesis). Accordingly, in the current clinical practice, this is arising as an important factor for prognostic evaluation of the effectiveness of the therapy for different kinds of tumors (2).

Currently, the reliability and the reproducibility of the functional results still represent an open issue, because of the high number of factors affecting the outcomes of CTp examinations, mainly due to examination protocols, acquisition artifacts, and methods of data processing and analysis (3). Importantly, the work by Miles et al. (4) emphasizes how these factors actually hamper the development of common standard guidelines for CTp. Among these factors, the motion artifacts of the patient can break the spatial fidelity of the imaged structures, causing inconsistent intensity trends for the generic spatial location of interest. Respiratory movements and tumor spatial heterogeneity can lead to mis-registrations in both transverse (x–y plane) and craniocaudal (z-axis) directions. These artifacts are more pronounced in the lower part of the thorax and in the upper part of the abdomen, thus giving, especially for liver and lung CTp, misleading impressions of rapid or slow inflow/outflow patterns to radiologists, and affecting the reliability of the resulting perfusion parameters. Generally, breath-hold acquisitions, as well as abdominal straps and antiperistaltic agents are commonly adopted to limit the movement of these structures (5), although even breath-hold acquisitions show variability (6). Nevertheless, several image

Acad Radiol 2014; 21:1416–1426

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http://dx.doi.org/10.1016/j.acra.2014.06.005

processing methods have been suggested in literature for motion compensation, mainly based on the post-processing of image data to perform registration to a reference data set. The impact of motion artifacts on CTp reproducibility for such methods is discussed for liver and lung tumors in (7,8), emphasizing how variability in the estimation of perfusion parameters can reach 70%–90% in the absence of any kind of compensation, while decreasing to relatively lower values (10%–20%) when data registration is applied. However, as reproducibility studies, the research by Ng et al. (7,8) do not mention the reliability of perfusion patterns, which were not even submitted for evaluation by radiologists.

Although using helical scanning, the three-dimensional (3D) rigid transformation model used by Ng et al. (7,8) was constrained to allow only shifting along axes. In general, the most complex methods use 3D registration of volumetric reconstructions from helical scanning in multiphase breath-hold acquisition protocols (9–12). These protocols aim at extending CT volume coverage (10,11) and exploit multidimensional reconstruction to perform a more accurate registration (12), but at the expense of a higher radiation dose being delivered to the patient (13), and without adding appreciable improvements in all cases where the lesion is often hidden and visible in few slices only. However, because of high temporal resolution and reduced dose delivery, axial scanning still remains the main technique recommended for CTp (5). Erroneous estimation of perfusion parameters for single tumor level (ie, fixed slice z-location) analysis is reported in the work by Bader et al. (14) and Nakashige et al. (15) for liver CTp, so that multi-level methods, based on retrospective visual selection of image sets contiguous to a reference z-axis position, are suggested (15,16). Manual translation of regions of interest (ROIs) (17) as well as and manual and anatomic-based image registration with respect to a reference slice are applied in lung (18) and liver (19) CTp, where motion effects can be even more evident.

However, some registration methods aim at assessing the effectiveness of image alignment only (18,19), or the reproducibility of perfusion parameters (7,8), although none of them, to our best knowledge, *measure* the effect of motion on TCC signal (ie, TCC's *reliability*), also correlating these measures with the reliability of perfusion analyses. Moreover, only few methods take into account x–y misalignments jointly with z-axis misalignments, meaning that a specific assessment of 3D manual registration is absent (18). As a matter of fact, very recent clinical studies are still conducted using x–y or craniocaudal compensation only (20), or not even that (21).

In this work, we expressly study and *measure* the effects of motion artifacts on TCCs and on the consequent reliability degree of perfusion colorimetric maps through a visual assessment by expert readers. To this purpose, we use a statistical error index referred to TCC *signal quality* and initially consider three different motion compensation approaches that must show increasing effectiveness: no compensation, x–y only, and 3D, which includes rigid shifting along the z-axis. In this way, it is easier to assess whether our quantitative index is really able to detect this expected increasing effectiveness, which would confirm its capability to correlate with quality of image alignments. For the sake of completeness, we also considered a fourth registration method (hereafter, 1D), aligning on the z-direction only, which is sometimes used in lung and liver perfusions (20). In addition, we submitted the sets of perfusion maps achieved for assessment by radiologists, so as to check if better alignments in any way yield more reliable color maps. In fact, if a better image registration expectingly brings more reliable TCCs on the available data, it cannot be taken for granted that these yield more reliable perfusion patterns in the color maps, also because alignments themselves might always introduce "regional artifacts." To this purpose, we analyze whether performing a 1D or a 2D alignment alone could in any case improve the reliability of perfusion maps, also discussing an interesting case in which both x–y and 3D alignments could produce different as well as reliable perfusion patterns.

Finally, it is worth noting that our approach can be used on both liver and lung tumors.

MATERIALS AND METHODS

The data set for this study was selected from a prospective CTp study, approved by the institutional review board, consisting of examinations regarding 18 patients with liver or lung tumors. All liver tumors were metastases, whereas all lung tumors were primary lesions. All patients had been instructed for breath-hold. However, to study and measure the effects of image registration on TCC and the computed perfusion parameters, we focused our attention on 11 patients (age range, 36–81 years) who had been able to hold their breath only partly. Accordingly, seven patients were excluded because their examinations were actually performed in breath-hold. All the examinations considered show residual breathing and undergo artifacts from motion requiring that, for each lesions, at least 25% of the slices of the reference sequence were replaced by slices relating to different z-levels. On the whole, each patient provided a different set of results for each of the four motion compensation approaches, for a total amount of 44 different configurations. Table 1 summarizes the 11 cases.

Perfusion CT Protocol

The patients' data sets were collected according to two different scanning protocols, depending on the investigated tissue. CT scans were performed on a 256-slice CT system (Brilliance iCT, Philips Medical Systems, Best, The Netherlands), with patients in the supine (feet first) position. An initial, low-dose, unenhanced, full-body CT scan was performed to identify the target lesions at baseline conditions. A 50-mL intravenous bolus of contrast agent (Iomeron, Bracco, Milan, Italy) was then injected at 5 mL/s for axial cine contrast-enhanced CT, according to two different protocols for liver and lung examinations.