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Research article

Quantification accuracy for dynamic contrast enhanced (DCE) CT imaging: phantom and quality assurance framework

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ABSTRACT

Purpose: Standardization and protocol optimization is essential for quantification of Dynamic Contrast Enhanced CT as an imaging biomarker. Currently, no commercially available quality assurance (QA) phantoms can provide for testing a complete set of imaging parameters pertaining to routine quality control for contrast-enhanced (CE) CT, as well as spatiotemporal accuracy. The purpose of this work was, therefore: (a) developing a solid calibration phantom for routine CE CT quality assurance; (b) investigating the sensitivity of CECT to organ motion, and (c) characterizing a volumetric CT scanner for CECT.

Methods: CECT calibration phantom consisting of an acrylic uniform cylinder containing multiple capsules of varying diameters and orientations was designed and built. The capsules contain different solid density materials mimicking iodine contrast enhancement. Sensitivity and accuracy of CECT measurements on all capsules was performed using a 320-slice CT scanner for a range of scan parameters both with and without phantom motion along the transaxial axis of the scanner.

Results: Routine commissioning tests such as uniformity, spatial resolution and image noise were successfully determined using the CECT phantom. Partial volume effect and motion blurring both contribute to a general decrease in contrast enhancement and this was further dependent on capsule orientation (least pronounced for the transaxial orientation). Scanning with a rotation time of less than 0.5 s, the effect of blurring is less than 3% for all orientations and phantom speeds.

Conclusion: A new robust contrast calibration phantom was developed and used to evaluate the performance of a 320-slice volumetric CT scanner for DCE-CT.

1. Introduction

Driven by numerus regulatory mechanisms, the principle task of the cardiovascular system and tissue microvasculature is the continuous tissue supply with oxygen and substrates as well as the elimination of metabolites. The ability to detect regional and global alterations in organ blood supply as well as tissue permeability is a major benefit of todays' non-invasive perfusion imaging techniques [1]. Among available imaging techniques for measuring tissue perfusion, is Dynamic Contrast Enhanced Computed Tomography (DCE-CT). With DCE-CT, the redistribution of a low molecular weight contrast agent after a bolus injection can be visualized and spatially as well as temporarily resolved (spatiotemporal sequence).

One potential important application of DCE-CT is the assessment of lesions within liver and lung parenchyma in order to distinguish benign changes from malignancy and delineate healthy tissue and/or fibrotic areas [2]. However, in order to apply DCE-CT techniques to organs exposed to continuous respiratory motion, reconstruction artifacts related to free-breathing acquisitions need to be taken into account [3]. Furthermore, motion-induced blurring will add temporal variations to the measured contrast enhancement values, possibly leading to quantification errors and artifacts in resulting parametric images.

Reducing such artifacts is no simple task and as such, DCE-CT imaging of the liver is typically performed under suspension of respiration (breath hold) whenever possible [2,4]. In principle, reconstruction artifacts from organ motion can be minimized with a high-temporal resolution, i.e. employing a high scanning frequency [5,6]. This is becoming feasible with current state-of-the-art multi-detector or dual-source CT systems that both enable high speed and increased coverage. A potential drawback of faster acquisition with a large FOV is

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a decreased image quality. The optimal scanning protocol that includes considerations about image quality and, at the same time, patient dose, may therefore not always employ the fastest gantry rotation time needed to minimize motion. As such, robust quantification at decreased image quality (lower dose) would be very desirable.

The linear relationship been CT contrast enhancement and contrast agent concentration is often quoted as a key feature making DCE CT an attractive perfusion imaging modality, which can easily be combined with anatomical CT information [7]. If this linear relationship is the same for both artery and tumor, the calibration of contrast concentration versus Hounsfield Unit (HU) is not required. However, especially within the chest this may rarely hold true, as beam hardening effects occur both due to high density contrast within the superior vena cava as well as air/tissue inhomogeneity and differences in patient size [8]. Within the framework of imaging biomarkers, accurate quantification and CT calibration of high atomic number contrast-enhancement (as from iodixanol) is paramount for evaluating response to treatment by repeated imaging [9]. As such, there is a clear need for not only calibrating the CT system for sensitivity to iodine in both relative and absolute terms, but also for assessing the stability of the calibration over time [10]. Although there are a variety of commercially available quality assurance (QA) phantoms, none can be used to extract a relatively complete set of imaging parameters pertaining to routine quality control procedures for contrast-enhanced (CE) CT and spatiotemporal accuracy required for motion-sensitive volumetric perfusion scans.

The purpose of this work, was therefore, to (a) develop a solid calibration phantom for routine contrast-enhanced imaging CT quality assurance; (b) investigate the sensitivity of contrast enhancement measurements to organ motion for a variety of acquisition parameters and (c) use this phantom to characterize a volumetric CT scanner for DCE-CT imaging.

2. Methods and materials

2.1. Contrast-enhancement calibration phantom design

Current methods of CT quality assurance (QA) are based on single-slice technology and guidance principles. In light of standardization efforts for quantitative imaging biomarker development, the RSNA is revisiting these recommendationsunder the Quantitative Imaging Biomarker Alliance (QIBA) working groups. In line with state-of-the-art CT technology, an ideal advanced phantom design for CT imaging should be able to:

- allow for helical, and cone beam imaging
- allow for larger field of view (FOV) for image guidance applications
- test respiratory motion – both gated and not gated
- test cardiac motion
- measure Quantitative HU (and/or densities) in the above applications
- use novel methods to measure patient dose
- test Dual energy CT and other quantitative imaging parameters (e.g. from DCE CT)
- look at failure modes (FMEA)
- test for iterative reconstruction
- provide artifact characterization

For DCE CT specifically, a Contrast Enhancement CT (CECT) phantom should provide a comprehensive set of imaging and quantification parameters applicable to DCE scanning and allow for routine quality control as well as protocol optimization with and without the presence of motion. Such a framework would also benefit the standardization of multi-center (multi-scanner) clinical trials involving DCE CT. Therefore, the initial design criteria for the CECT phantom were as follows:

1 HU accuracy for robust quantification
2 Volume definition - for measurement of arterial input function (AIF)
3 Spatial resolution – including orientation dependence of vessels
4 3D modulation transfer function (MTF)
5 Image quality
6 Temporal resolution - sensitivity to motion.

The resulting phantom design consists of an acrylic cylinder containing 48 high density capsules of fixed 20 mm length, and varying diameters (1, 2, 5 and 10 mm) and orientations (transaxial, diagonal and axial) at predefined positions. Solid materials were chosen instead of prepared contrast concentration solutions [11] as the latter will evaporate over time and are prone to variations in preparation, therefore making it unsuitable for a robust QA program. The use of solid materials is also more flexible to adjust the material composition to provide tissue-specific attenuation according to beam energy (thinking ahead to dual-energy CT). The range of capsule materials was chosen to mimic different levels of contrast-enhancement when converted from concentration (mg/ml) to signal (HU) following contrast injection in clinical DCE-CT protocols [4,12] and provide a worst-case scenario analysis in terms of image artifacts and partial volume effects. They are arranged in such a way as to minimize the number of high-density objects in any one plane potentially causing reconstruction artifacts. Typical physiological concentrations of iodixanol found in tissues and vessels after IV bolus injection will range between 1.5 to 15mgI/ml. Four materials were used to mimic a matching contrast enhancement, giving a range of CT numbers up to 250 HU. Details of the capsule compositions, electron densities and characteristics are listed in Table 1. The relative electron density is the major determinant of the level of Compton interactions

The capsules were categorized into four groups based on material compositions and electron density, making HU calibration analysis easily applicable. In each group, capsules with different diameters were used to test volume definition based on threshold-HU segmentation. Three directions of capsules would reveal the orientation dependence of average and standard deviation of CT numbers, making HU analysis accurate and robust.

The orientations were defined with respect to the plane of the rotating gantry of the CT scanner (see Fig. 1): A capsule in the transaxial orientation was oriented with its long axis along the z-axis, whereas a capsule oriented axially was oriented with its long axis in the x–y plane. The diagonal orientation denotes a capsule axis drawing an angle of 45° with respect to the x–y plane.

2.2. CT data acquisition

2.2.1. Static phantom

CT imaging was performed on a 320-slice Aquilion ONE scanner (Toshiba, Tochigi Pref., Japan). The CECT phantom was positioned on the patient table with its long axis aligned with the z-axis and its central positioning confirmed by positioning lasers (see Fig. 1). All images were acquired in Volume Mode settings with no table movements employing 0.5 mm slice collimations (volume coverage: 320 × 0.5 mm = 160 mm) with variable scan parameters as described in the following sections. Image uniformity had been verified previously and found to be within

Table 1
Overview of insert material properties.

Material	Formula	Physical Density (g/cm^3)	Relative Electron Density	Effective Atomic Number
Polystyrene	(C8H8)n	1.05	1.02	5.70
Ultem	(C37H24O6N2)n	1.27	1.19	6.30
Delrin	(CH2)n	1.41	1.36	6.95
Torlon	(C21H12O4N2)n	1.56	1.48	6.40