Evaluating the Feasibility of C-arm CT for Brain Perfusion Imaging: An *in vitro* Study

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ABSTRACT

C-arm cone-beam CT (CBCT) is increasingly being used to supplement 2D real-time data with 3D information. Temporal resolution is currently limited by the mechanical rotation speed of the C-arm which presents challenges for applications such as imaging of contrast flow in brain perfusion CT (PCT). We present a novel scheme where multiple scans are obtained at different start times with respect to the contrast injection. The data is interleaved temporally and interpolated during 3D reconstruction. For evaluation we developed a phantom to generate the range of temporal frequencies relevant for PCT. The highest requirements are for imaging the arterial input function (AIF) modeled as a gamma-variate function. Fourier transform analysis of the AIF showed that 90% of the spectral energy is contained at frequencies lower than 0.08Hz. We built an acrylic cylinder phantom of diameter 1.9 cm, with 25 sections of 1cm length each. Iodine concentration in each compartment was varied to produce a half-cycle sinusoid variation in HU in version 1, and 2.5 cycles in version 2 of the phantom. The phantom was moved linearly at speeds from 0.5cm/s to 4cm/s (temporal frequencies of 0.02Hz to 0.09Hz) and imaged using a C-arm system. Phantom CT numbers in a slice reconstructed at isocenter were measured and sinusoidal fits to the data were obtained. The fitted sinusoids had frequencies that were within 3±2% of the actual temporal frequencies of the sinusoid. This suggests that the imaging and reconstruction scheme is adequate for PCT imaging.

Keyword list

Perfusion CT (PCT), stroke, C-arm, temporal resolution, sinusoidal phantom, frequency content.

1. INTORDUCTION

The standard of care for evaluating patients who have stroke-like symptoms involves an initial conventional CT scan. Stroke can be hemorrhagic or ischemic in nature though approximately 85% of strokes are ischemic in origin[1]. In a majority of these cases even when imaging is performed within 6 hours of the onset of symptoms, a conventional CT scan can be normal or could show only subtle traces of abnormalities which are difficult to assess. To get a more accurate diagnosis, perfusion CT is performed as a follow up to the initial scan. Perfusion CT requires the administration of a bolus of iodinated contrast agent followed by continuous imaging of the CT slices of concern from the arrival to the wash out of the contrast agent. Such CT perfusion data can positively identify non-hemorrhagic stroke and allow selection of patients who would benefit from thrombolytic treatment or localized vascular therapies. Systemic thrombolytic treatment can be administered in a limited time window of only 3-6 hours from symptom onset, beyond which complication rates increase significantly[2, 3]. Local vascular therapies, including arterial delivery of clot busting drugs such as tissue plasminogen activator (tPA) or mechanical thrombectomy, may have a longer time window following stroke onset during which they can be safely applied. These minimally

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invasive treatments are conducted under real-time image guidance using x-ray angiographic systems, and use the results of these prior CT studies for guidance. Typically no further perfusion guidance is available to evaluate the completion and success of the therapy because of work flow issues and the short time window offered. Availability of perfusion information using the C-arm system ie. without moving the patient onto another imaging platform, could potentially improve the safety and efficacy of the interventional therapeutic procedures.

High-end angiographic systems consist of an x-ray tube and a digital x-ray detector mounted on a C-arm. In addition to providing real-time (30 frames/s) 2D projection images, recent developments in the field allow acquisition of 3D volume images using such systems[4]. This is also known as C-arm cone-beam CT (CBCT). When acquiring data for 3D reconstruction, the detector can currently image at 60 frames/s uisng a 4x4 binned-pixel mode with a resolution of 1 lp/mm. The biggest limitation with respect to imaging perfusion using a C-arm system is the slow rotation speed of the arm which rotates at a speed that is an order of magnitude slower than the rotation speed of a clinical CT system (~5s for C-arm CBCT compared to ~0.5s for conventional CT). Additionally, the C-arm rotates in a bi-directional fashion from scan to scan with finite turn-around times (~1s) between successive scans. Other authors[5] have investigated the feasibility of using C-am systems for measuring the cerebral blood volume (CBV) which is a perfusion CT parameter that measures the fraction of blood per unit tissue mass. Using a long two-step injection followed by a special image processing scheme they were able to avoid the temporal resolution limitations of the C-arm system for measuring CBV. However, the other critically important parameter in perfusion imaging, the cerebral blood flow (CBF) maps, cannot be calculated using such a scheme. We propose a targeted image acquisition and reconstruction scheme that should potentially allow us to use a C-arm CBCT system to measure both CBF and CBV during perfusion imaging.

The method for modifying the C-arm image acquisition and reconstruction pipeline for enabling CBF measurements involves acquiring multiple acquisitions at different time delays with respect to injections of iodinated contrast agent. This results in availability of reconstructed volumes at intervals that are shorter than for a single injection followed by scans. The data acquired from these multiple scans is re-arranged to be sequential and a reconstruction algorithm is then applied. The initial evaluation of the accuracy of this method was evaluated using our sinusoidal frequency phantom. Below we present an overview of our image acquisition and reconstruction method and details of the feasibility studies using phantoms.

2. MATERIALS AND METHOD

2.1 Imaging System Description

For our imaging study we used a C-arm CBCT system (Axiom Artis dTA and DynaCT, Siemens AG, Forchheim, Germany). It uses a 30cm x 40cm indirect detection flat panel detector which images at 60 frames/s during 3D acquisition. The fastest rotation time of the C-arm is 4.30s with a turn-around time of 1.25s. Currently in the multi-sweep mode, it allows six consecutive bi-directional rotations where each rotation results in a 3D volume image. The imaging system used in this study is shown in **Fig. 1**.

2.2 Imaging Considerations for Stroke

For perfusion imaging during stroke, the parameter that requires the highest temporal sampling is the arterial input function (AIF). The AIF is needed to normalize the perfusion results to remove the effect of the shape and timing of the bolus injection on the final measurements. The arterial function can have a full width at half maximum (FWHM) of between 2-8 s [6, 7] and is typically modeled as gamma-variate function. It has a functional form shown below[8, 9]:

$C(t) \ \alpha \ t^3 \cdot \exp(-t/a)$ (1)

where a is 1.5 for an intra-venous (IV) injection and is 1 for an intra-arterial (IA) injection (**Fig 2**). Typically for imaging cerebral perfusion using a conventional CT scanner, an intra-venous injection is delivered. However, it is

Figure 1. C-arm CBCT system used for imaging in this study.

conceivable that for C-arm CBCT imaging, an intra-arterial injection could be administered since the patient is already catheterized for vascular therapy. The advantage of an intra-arterial (IA) injection is that it might be possible to gain the same enhancement as with an intra-venous (IV) injection with potentially a much smaller volume of iodinated contrast given that it would not have to undergo systemic dilution as with an IV injection. However as is evident from **Fig 2(a)**, this requires better temporal sampling compared to the IV injection.

In order to investigate the timing requirements for adequately sampling the AIF functions, we performed a Fourier transform of the gamma-variate function. An analysis of the spectral energy of the Fourier data shows that approximately 90% of the energy in the signal is contained between 0-0.06 Hz and 0-0.08 Hz for IV and IA injections respectively (**Fig 2(b)**). In fact data from human CT scans have shown that 90% of the spectral energy lies within 0.05 Hz for IV injections and up to 99% lies within 0.15 Hz even for a conservative estimate[10]. Hence for assessing the accuracy of the C-arm CBCT system for measuring AIF during perfusion studies, we designed a phantom that generates various temporal frequencies which were imaged and processed for analysis.

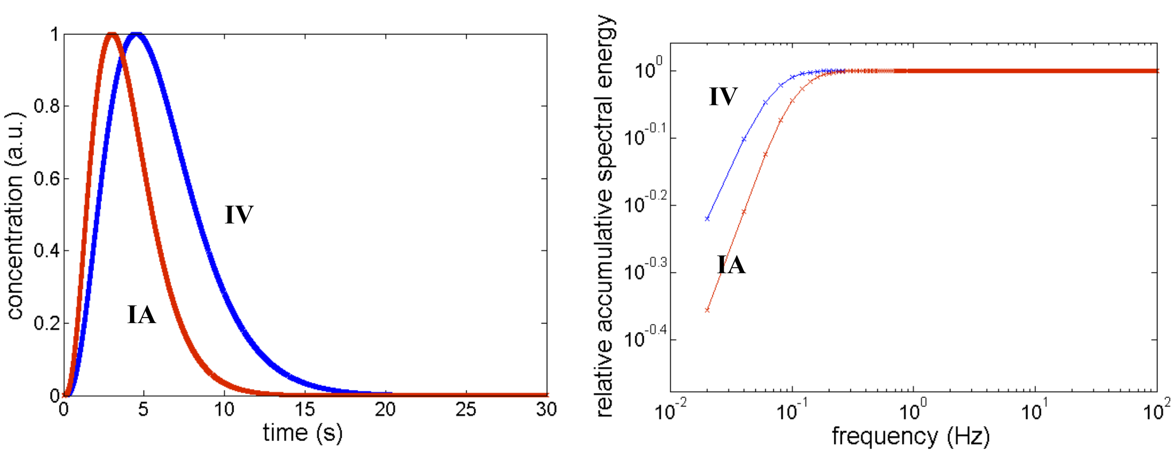
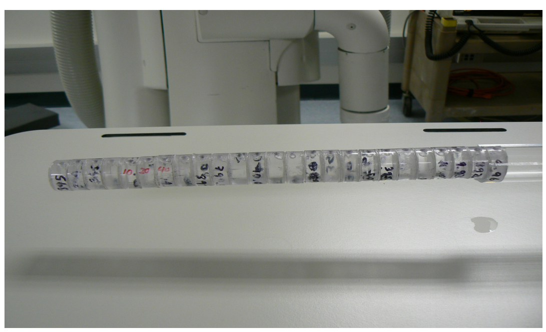


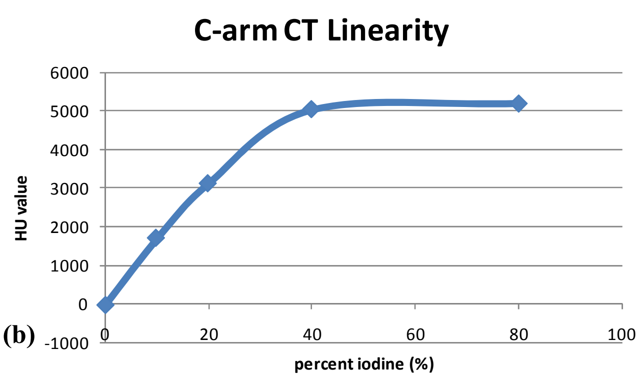
Fig 2(a). AIF for IV (blue) IA (red) injection **(b)** Relative accumulated spectral energy for IV (blue) IA (red) injections.

2.3 Phantom Design

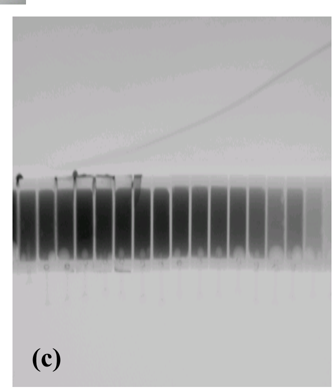
For assessing the ability of the C-arm CBCT system to image various temporal frequencies, we designed a sinusoidal phantom. This derives its basis from the fact that any signal, in this case the AIF, can be expressed as a sum of sinusoids in the frequency domain. The sinusoidal image pattern was created by dividing an acrylic cylinder into twenty-five 1cm compartments each with 1.9 cm diameter **Fig 3(a)**. The compartments were filled with iodinated contrast with the percentage of iodine in each being adjusted so that one half of a sinusoid was covered between the two ends of the cylinder. To determine the range of contrast concentrations to be imaged, the linearity curve for the C-arm CBCT system as a function of iodine concentration was determined (**Fig 3(b)**). The iodine contrast used contained 300 mgI/ml (Omnipaque, GE Healthcare, WI). The peak of the sinusoid was filled with 40% iodine with the intermediate steps on either side going down to 0% in steps that define the sinusoid. The phantom was then mounted on a linear stage that was driven by a linear motor along the axis of rotation of the C-arm. An x-ray projection image of the phantom is shown is **Fig 3(c)**. By changing the linear velocity, sinusoids of different frequencies were generated. The linear velocities at which the phantom was imaged ranged from 0.5 cm/s to a maximum of 4 cm/s. Given the length of 28 cm for the length of the phantom and the fact that this corresponded to half the wavelength, the maximum frequency imaged was 0.07 Hz. Subsequently we also imaged an improved version of the phantom where the peak value of the sinusoid was set to between 500-600 HU which is more clinically relevant in terms of perfusion CT. In this phantom the contrast agent concentration was adjusted such that two and a half complete sine waves could be accommodated within the 25 compartments with a total length of 27.34 cm. This allowed us to increase the highest frequency imaged with the same maximum linear velocity of 1 cm/s to 0.1 Hz. Also in this case we oscillated the sinusoidal phantom back and forth in a cylindrical cavity inside a 10 cm acrylic cylinder that was filled with water. This provided similar attenuation and scatter to a head. Back and forth oscillations were desired so that the imaging system saw the phantom at all times during all scans.

(a)





(b)



(c)

Fig 3(a). Cylindrical phantom with equi-spaced partitions containing iodinated contrast of varying concentrations **(b)** Linearity of C-arm CBCT as a function of iodine concentration **(c)** A projection image of a segment of the phantom containing iodine concentration with sinusoidal variations.

2.4 Image acquisition protocol

As mentioned in the system description, the C-arm CBCT system generates one 3D volume in 4.3s, followed by a gap of 1.25s when the arm turns around, and then the next volume is acquired. Six such consecutive data samples can be acquired in one scan (Scan A **Fig. 4**). In case of perfusion imaging this would result in sparse sampling of the time density curves following injection of contrast agent. This would cause severe under-sampling of the AIF. The tissue enhancement curves might be less affected since they are broader than the AIF. However the resulting CBF values would be highly inaccurate. One method for increasing the temporal sampling could be to use multiple scans that start at different delays with respect to the start of the injection. Such an imaging scheme is shown in **Fig. 4** where the different symbols stand for the different scans. Each scan generates 6 data points by using 6 consecutive bi-directional sweeps. By considering the total duration of scan for perfusion CT (40-50s post contrast injection) and the number of sub-samples desired, we chose to acquire 6 sets of scans (scans A-F). The different delays relative to the start of the scan were optimized and set to be -4.6, -2.8, -0.9, +0.9, +2.8 and +4.6s, respectively for the six scans. Though this method increases the number of sample points along the curve, each reconstructed data set is, however, an average of the dynamics that happen over the 4.3s during which each sweep is completed. To compensate for this effect we use a specific image processing and reconstruction method described below.

2.3 Imaging reconstruction algorithm

The image reconstruction algorithm involved first reorganizing the acquired projection datasets from the 6 scans (each containing data from 6 sweeps) such that the datasets were sequential. Reconstruction of the data was based on an extension of the work by Montes *et al*[10, 11]. Briefly this involves dividing the data from one sweep into several equiangular blocks which in our case was optimized to be 6 blocks. Initial back projection of these blocks is performed followed by interpolation of values between blocks for each voxel assuming a smooth contrast-induced temporal enhancement function. The data acquired during the C-arm CBCT acquisition is irregularly sampled given the bi-directional sweep with finite turn-around. In this work linear interpolation was used for regular sampling[12].

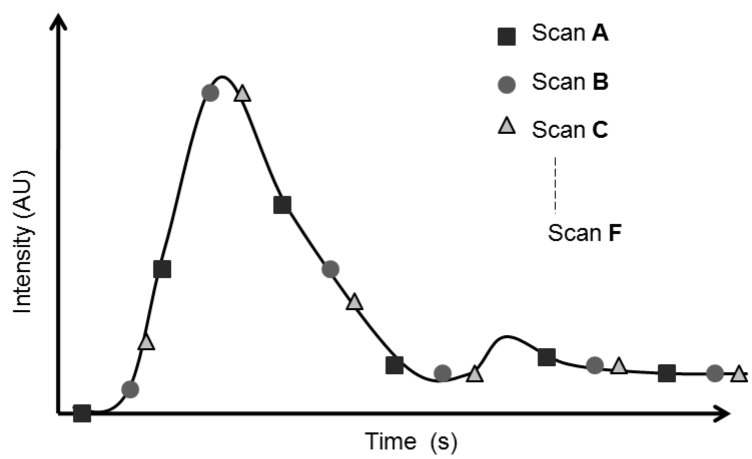


Fig 4. Schematic of multi-scan protocol where each scan (A-F) consists of 6 sweeps generating 6 volumes or data points per scan.

2.4 Image analysis

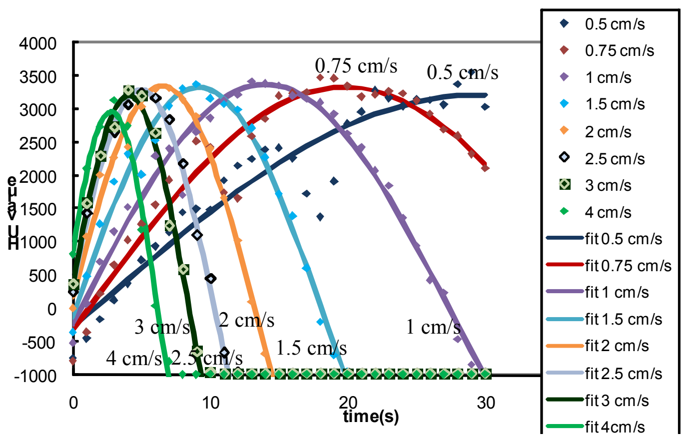
At each linear velocity of the sinusoidal phantom, 6 data sets (each containing data from 6 sweeps) were acquired at the different optimized delays defined above. Image slices near the iso-center of the imaging volume were reconstructed at 0.5 mm thickness using the modified algorithm. A 10 pixel x 10 pixel square region of interest (ROI) at the center of the phantom image was analyzed and the HU values were plotted as a function of time. The data for each linear velocity was then fitted to a sinusoid using a least-squares method. The frequency of the fitted sinusoid was then compared to the physical frequency of the wave that was calculated by dividing the linear velocity by the wave length of the sinusoidal phantom.

3. RESULTS

Figure 5(a) shows the results from imaging the first phantom at different velocities. The peak value of the sinusoid appeared to decrease with increasing velocities. There was a total decrease of 12% from the peak for 0.5 cm/s to 4 cm/s. The error in calculating the frequency of the sinusoid from the fit to the data compared with ground truth was 3.46(±2.42) %.

Figure 5(b) shows the results of imaging the improved phantom. The errors in matching the fitted frequencies with ground truth were 3.14% and 6.89% respectively for 0.5 cm/s and 1 cm/s. The scatter in the data was larger in this case since fewer data points were available per cycle. Also although the turnaround time of the phantom was in the sub-second range it caused errors in the latter half of the data when the phantom reversed its direction of travel.

(a)



(b)

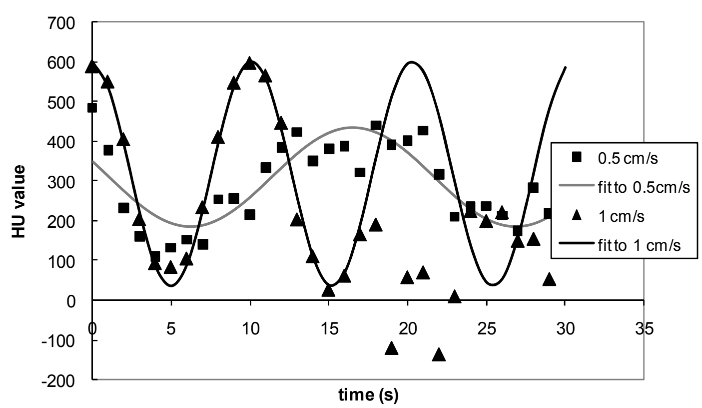


Fig 5. Fitted sinusoids of different frequencies for data obtained by imaging the sinusoidal contrast phantom at different velocities **(a)** for initial phantom that was imaged in air **(b)** for phantom that includes realistic parameters during imaging of stroke.

4. CONCLUSIONS AND DISCUSSION

From the above results it can be concluded that by using our C-arm CBCT system along with the modified image acquisition and reconstruction scheme, a majority of the temporal frequencies involved in perfusion CT imaging are adequately sampled. This is a significant finding as this enables the possibility of measuring CBF using the C-arm CBCT system. Further work to analyze how the accuracy of the results changes with reducing the number of scans to below six is currently underway. This analysis will be carried out by using a subset of the scans from the dataset already acquired with the phantom, during the reconstruction process. This study was intended to demonstrate proof of concept, and did not consider dose/signal-to-noise/temporal resolution trade-offs. Further investigations to determine the minimum number of acquisitions required and the minimum dose per acquisition to accurately represent the AIF and VIF are underway.

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