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An Enhanced SMART-RECON Algorithm for Time-Resolved C-arm Cone-Beam CT Imaging

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Abstract

Temporal resolution in time-resolved cone-beam CT (TR-CBCT) imaging is often limited by the time needed to acquire a complete data set for image reconstruction. With the recent developments of performing nearly limited-view artifact-free reconstruction from data in a limited-view angle range and a prior image, temporal resolution of TR-CBCT imaging can be improved. One such an example is the use of Simultaneous Multiple Artifacts Reduction in Tomographic RECONstruction (SMART-RECON) [1] technique. However, with SMART-RECON, one can only improve temporal resolution up to 1 frame per second (fps) which is an improvement of 4.5 times over that of the conventional FBP reconstruction. In this paper, a new technique referred to as enhanced SMART-RECON (eSMART-RECON) was introduced to enhance the temporal performance of SMART-RECON in a multi-sweep CBCT data acquisition protocol. Both numerical simulation studies with ground truth and *in vivo* human subject studies using C-arm CBCT acquisition systems were conducted to demonstrate the following key results: for a multi-sweep CBCT acquisition protocol, eSMART-RECON enables 4–7.5 fps temporal resolution for TR-CBCT which is 4–7.5 times better than that offered by the original SMART-RECON, and 18–34 times better than that offered by the conventional FBP reconstruction.

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Index Terms—

C-arm CBCT; Time-resolved imaging; Temporal resolution; Image Reconstruction

I. Introduction

Clinical time-resolved volumetric CT imaging can be implemented using either a diagnostic multi-detector row CT (MDCT) scanner or a flat-panel based cone beam CT (CBCT) system commonly used in image-guided interventions and image-guided therapy. The primary motivation of this paper is the application of CBCT in the diagnosis and image-guided intervention/treatment of vascular diseases.

A. Clinical motivation for time-resolved cone beam CT (TR-CBCT) imaging in interventional suite

Since the introduction of digital subtraction angiography (DSA) [2]–[4] into clinical practice in the 1980s, this two-dimensional time-resolved x-ray imaging technique has become an indispensable imaging tool in interventional suites. DSA remains the clinical gold standard for the diagnosis of many vascular diseases such as occlusions, stenoses, and aneurysms. However, an intrinsic limitation of any two-dimensional DSA (2D-DSA) is the superposition of anatomy at different depths along the x-ray paths. For example, the superposition of vasculature in the subtracted images may impede the visualization of vasculature or the diagnosis of vascular pathologies. To provide fully three-dimensional (3D) visualization and understanding of spatial structure of vasculature, a series of rotational 2D-DSA images can be acquired and tomographically reconstructed to generate 3D rotational DSA (3D-DSA) [5]–[9]. The introduction of 3D-DSA addresses the problem of structural superposition in 2D-DSA, but with a cost of losing the time-resolving capability of 2D-DSA. Thus, 3D-DSA imaging has severe limitations for certain clinical needs such as the identification of antegrade or retrograde filling of feeding arteries, collateral circulation assessment, or differentiating feeding arteries from draining veins in patients with cerebral vascular malformations, including arteriovenous malformations, arteriovenous fistulas, and developmental venous anomalies.

The purpose of this paper was to present and validate an iterative image reconstruction technique to achieve time-resolved CBCT imaging with 4–7.5 frames per second (fps) temporal resolution without noticeable limited-view artifacts, when the reconstruction technique is combined with a multi-sweep contrast-enhanced CBCT acquisition protocol.

In terms of temporal resolution, spatial resolution, and spatial coverage along the superior/inferior (S/I) direction, some state-of-the-art MDCT systems also offer similar technical specifications to that of the C-arm CBCT system equipped with the proposed eSMART-RECON technique, i.e., 4–7.5 fps frame rate and 0.3 mm spatial resolution. For example, the Canon's Aquilion One or GE's Revolution 256-slice scanners can provide 16 cm spatial coverage along the S/I direction. With the state-of-the-art gantry rotation speed of about 300 ms, these systems can provide a temporal resolution of about 150 ms, i.e., 6.7 fps frame rate.

These systems offer a spatial resolution of 0.5 mm at the iso-center and some systems can even offer 0.25 mm spatial resolution for certain clinical applications.

However, the MDCT systems are not designed to provide image guidance for interventional procedures that require the availability of real-time 2D x-ray vascular images at any physician preferred gantry angle and a system design to meet the safety requirement for both patient and medical personnel in the interventional suite. In contrast, the C-arm gantry based imaging systems are specifically designed to meet these requirements. As a result, the C-arm gantry speed for image acquisitions must be slow which fundamentally limits its temporal resolution in tomographic imaging for soft tissues to be less than 0.2 fps for a five second per rotation gantry speed. This is a stark contrast to the temporal resolution for 2D x-ray projection imaging that can be as high as 30 fps. The eSMART-RECON technique presented in this paper provides a potential technical solution to address this limitation on temporal resolution in C-arm CBCT perfusion and time-resolved CBCT angiography.

B. Review of currently available techniques for TR-CBCT

Several technical schemes have previously been proposed to address the potential challenges in CBCT perfusion and time-resolved CBCT angiography imaging. One scheme was to use two interleaved CBCT perfusion scans [10], with the second scan having a different x-ray delay time after contrast injection, potentially doubling the temporal sampling density. Another scheme [11]–[14] was to decompose the time attenuation curves (TACs) of different image voxels in terms of known temporal bases such as Gaussian functions, gamma-variate functions, linear splines, or cubic splines. The incorporation of known basis functions in this scheme dramatically reduces the number of unknowns, hence, strongly regularizes the ill-posed optimization problem. In the third scheme, a temporal deconvolution method was proposed in [15]–[17] to improve the temporal sampling density and temporal resolution in CBCT imaging by deconvolving the measured TAC with a known convolution kernel. In the fourth scheme, the so-called local attenuation curve optimization (LACO) framework was proposed [18] to accurately model the TACs inside the vessel regions and optimize the TACs constrained by the acquired projection data.

C. TR-CBCT via limited-view angle reconstruction method

Since the temporal information content of a given image is determined by the temporal information encoded into the acquired projection data, the temporal resolution of a tomographic imaging system is determined by the temporal window to acquire the needed projection data set for an image reconstruction method. Given the fact that different CT image reconstruction methods may have different requirements on data usage, the temporal resolution of a tomographic imaging method is jointly determined by the data acquisition speed and the image reconstruction methods. For a given data acquisition speed (determined by the available gantry rotation speeds, detector readout speed, and specific acquisition protocol), the achievable temporal resolution is bounded by the temporal window of data usage in image reconstruction. If one can manage to reconstruct a single image frame from projection data from a reduced temporal window without introduction of limited-view artifacts in the reconstructed image, then the temporal resolution is effectively reduced. This

is the basic idea behind the attempts to use iterative image reconstruction methods to improve temporal resolution while suppressing limited-view artifacts [1], [19]–[21].

One such method is the Simultaneous Multiple Artifacts Reduction in Tomographic RECONstruction (SMART-RECON) [1] technique. Using the SMART-RECON technique, it was demonstrated [22] that one can reconstruct time-resolved image volumes from a single short-scan CBCT acquisition to improve temporal resolution. Specifically, up to five image frames with clear temporal variation can be reconstructed without introducing limited-view artifacts from a single short-scan data acquisition. Therefore, the best performance of the current SMART-RECON is to obtain a temporal resolution of about one frame per second (1.0 fps) which is 4.5 times better than that offered by the conventional FBP reconstruction [23]. With the constraint of a single short-scan cone beam CT acquisition, it would be very difficult to further improve of temporal resolution using SMART-RECON since it is difficult to balance the need to eliminate limited-view artifacts while maintaining the needed temporal fidelity simultaneously.

D. Major innovations in this paper

The ultimate goal of time-resolved imaging is to provide a detailed delineation of temporal dynamics of the image object over a given clinically relevant temporal window. For time-resolved vascular imaging, the goal is to generate temporal snapshots of vasculature over the entire time course of contrast uptake with an intravenous (IV) contrast injection protocol. A typical data acquisition window is about 30 seconds. Within this acquisition window, one may capture the early arterial phase, peak arterial phase, and late venous phase of contrast medium in vasculature. Given the current data acquisition speed for a C-arm cone beam CT system in interventional suite, to acquire sufficient data to cover the time course of the contrast media in vasculature, the C-arm gantry must perform 8–10 back-and-forth C-arm CBCT acquisitions. Additionally, to mechanically reverse the gantry rotation direction, a pause period of about 1 second without data acquisition is needed. As a result, as described in literature [16], [24], the acquired TR-CBCT data set consists of multiple short-scan CBCT projection data sets over a temporal window of 30–60 seconds.

The major innovation in this paper was to present a new enhanced SMART-RECON technique, which will be referred to as eSMART-RECON in this paper, to significantly improve temporal resolution for this type of multi-sweep time-resolved data acquisition protocol. The key innovation in the eSMART-RECON technique was motivated by the following observations: Limited-view artifacts are strongly dependent on the angular span and the relative orientation of the view angle span to the image object. In a single sweep CBCT acquisition, the severity and orientation of the limited-view artifacts are different from one angular sector to another. However, when a multi-sweep data acquisition protocol is utilized and the angular sub-sectors used within each sweep are similar, the severity and orientation of the limited-view artifacts for a specific view angle sector in a given short-scan data set will repeatedly appear in those angular sectors with the same relative orientation to the image object in other short-scan data sets. Therefore, the limited-view artifacts in a multi-sweep acquisition protocol demonstrate a temporally periodic pattern. It is this prior

knowledge that will be properly incorporated into the original SMART-RECON method to further improve the temporal resolution of TR-CBCT imaging.

II. From SMART-RECON to eSMART-RECON

A. Notation of spatial-temporal image matrix in TR-CBCT

Suppose a multi-sweep TR-CBCT acquisition consists of a total of T_s sweeps of short-scan CBCT acquisitions. Each short-scan CBCT projection dataset is retrospectively sorted into T' non-overlapping angular sub-sectors, and each sub-sector corresponds to a specific time frame. The reconstructed CBCT image corresponding to the i -th time frame is denoted by an image vector $\vec{X}_i (i = 1, 2, \dots, T = T'T_s)$. These image vectors are combined into a spatial-temporal image matrix $\mathbf{X} = (\vec{X}_1, \vec{X}_2, \dots, \vec{X}_T)$.

B. A brief review of SMART-RECON method

As previously shown [1], the SMART-RECON algorithm was formulated to solve the following convex optimization problem:

$$\tilde{\mathbf{X}} = \arg \min_{\mathbf{X}} \left[\frac{1}{2} (\vec{\mathcal{Y}} - \mathcal{A}\mathbf{X})^T \mathcal{D} (\vec{\mathcal{Y}} - \mathcal{A}\mathbf{X}) + \lambda \|\mathbf{X}\|_* \right], \quad (1)$$

where $\vec{\mathcal{Y}}$ denotes the vectorized projection data arranged by time frames, and $\vec{\mathbf{X}}$ denotes the vectorized spatial-temporal image matrix $\mathbf{X}$. $\mathcal{A}$ denotes the modified system matrix according to the data partition scheme in preceding subsection. $\mathcal{D}$ denotes the statistical penalty matrix which is a diagonal matrix with the detector counts as its non-zero entries. λ denotes the regularization strength.

The convex optimization problem in Eq. (1) was solved in the following alternating steps [1]:

$$\vec{\mathbf{X}}^{(k)} = \vec{\mathbf{X}}^{(k-1)} + \delta \mathcal{A}^T \mathcal{D} \left[\vec{\mathcal{Y}} - \mathcal{A} \vec{\mathbf{X}}^{(k-1)} \right], \quad (2)$$

$$\mathbf{X}^{(k+1)} = \arg \min_{\mathbf{X}} \frac{1}{2} \|\mathbf{X} - \mathbf{X}^{(k)}\|_F^2 + \lambda \|\mathbf{X}\|_*, \quad (3)$$

where δ denotes the updating step size. It was empirically fixed to 0.25 in this study. $\|\cdot\|_F$ denotes the Frobenius norm of a matrix, $\|\cdot\|_*$ denotes the nuclear norm of a matrix, and $\mathbf{X}^{(k)}$ denotes the reconstructed image in the k -th iteration. The solution of the nuclear norm minimization problem is given by the singular value thresholding (SVT) operator given below [25]:

$$\text{SVT}_\lambda(\mathbf{X}) = \mathbf{U}(\Sigma - \lambda \mathbf{I})_+ \mathbf{V}^T, \quad (4)$$

$$[(\mathbf{\Sigma} - \lambda \mathbf{I})_+]_{r,r} = \begin{cases} \sigma_r - \lambda, & \sigma_r \geq \lambda \\ 0, & \sigma_r < \lambda \end{cases} \quad (5)$$

where $\mathbf{U}$, $\mathbf{V}$, and $\mathbf{\Sigma} = \text{diag}\{\sigma_1, \sigma_2, \dots, \sigma_T\}$ denote the singular value decomposition (SVD) of $\mathbf{X}$, and $\mathbf{I}$ is an identity matrix.

C. Periodicity of limited-view artifacts in TR-CBCT with a multi-sweep acquisition protocol

As previously mentioned, multi-sweep acquisition protocols offer a new opportunity to generate prior knowledge for limited-view artifacts reduction in SMART-RECON technique. In this subsection, we present an example to highlight this key observation. Data acquired from *in vivo* human subject studies were used for illustration purposes (data acquisition details are presented in section III-B). The 8 contrast filled datasets (CBCT acquisition with contrast injection) acquired using a 10-sweep acquisition protocol were partitioned into 40 equiangular sub-sectors. For each angular sub-sector, a simple least squares-based reconstruction was used to generate images with limited-view artifacts. These 40 image volumes were used to generate the spatial-temporal matrix $\mathbf{X}$. The SVD was applied to the image matrix to decompose the image matrix, i.e., $\mathbf{X} = \mathbf{U}\mathbf{\Sigma}\mathbf{V}^T$. Here $\mathbf{U}$ and $\mathbf{V}$ are orthogonal matrices, and $\mathbf{\Sigma}$ is a diagonal matrix with singular values as its diagonal entries. Fig. 1 shows eight (every fifth) reconstructed image frames (top row), the first eight spatial bases (second row), and the first eight temporal bases (third row).

To detect the potential periodicity of artifacts presented in these 40 angular sectors, Fourier analysis was performed over the temporal basis images and results were presented in the bottom row of Fig. 1. Here the amplitudes of the discrete Fourier transform (DFT) of the temporal bases are presented. As shown in this example, temporal bases V_2 , V_6 , V_7 , V_8 demonstrated strong quasi-periodic oscillations. These oscillations also appear in the corresponding Fourier spectra, which peak at the temporal frequencies at $0.0962/s$ (V_2 basis), $0.2886/s = 3 \times 0.0962/s$ (V_7 basis), and $0.5772 = 6 \times 0.0962/s$ (V_6 and V_8 bases) as highlighted by red vertical lines Fig. 1.

These plots lead to the following key observation: since, the data acquisition time for each sweep is $t_s = 5.2$ s, and the acquisition is performed by repeating forward and reverse rotations about the image object in a back-and-forth manner, the limited-view angle artifacts should exhibit a periodic pattern with a fundamental temporal frequency of $\pm \frac{1}{2t_s}$ and higher

order harmonics at $\pm n \frac{1}{2t_s} (n = 2, 3, \dots)$. In other words, *if the peak spectral energy in a temporal basis falls onto these characteristic temporal frequencies, then the corresponding spatial and temporal bases can be identified with the bases that are dominated by the limited-view artifacts*. When $t_s = 5.2$ s, one obtains the corresponding fundamental frequency and higher order harmonics at $\pm n \frac{1}{2t_s} = \pm 0.0962/s \times n$. Therefore, in the example shown in Fig.

1, the bases V_2 , V_6 , V_7 , V_8 can be identified as the bases that are dominated by the limited-view artifacts, since the peak spectral energy falls onto characteristic temporal frequencies.

The above empirical observations can be formulated as a criterion to identify limited-view artifacts in SMART-RECON. Specifically, if the r -th temporal bases, V_r is dominated by the limited-view artifacts, it can be identified by using the following criterion:

$$\left\{ r \mid |\mathcal{F}(V_r)|\left(\frac{n}{2t_s}\right) \geq \gamma |\mathcal{F}(V_r)|_{\max} \right\}, \quad (6)$$

where, $n = \pm 1, \text{ or } \pm 2, \text{ or } \pm 3, \dots \text{ or } \pm T'$. $\mathcal{F}(\cdot)$ denotes the DFT operation and $|\mathcal{F}(V_r)|(f)$ denotes the amplitude of the Fourier spectrum of V_r at a temporal frequency f . $|\mathcal{F}(V_r)|_{\max}$ denotes the maximal amplitude of the spectrum of V_r . γ denotes a relaxation parameter to define the peak Fourier spectral energy. For simplicity, $\gamma = 1$ was used in both numerical simulation studies and human subject studies throughout this paper.

D. Proposed eSMART-RECON: Algorithm and Numerical Implementation

In this paper, the performance of the SMART-RECON technique in TR-CBCT application with a multi-sweep acquisition protocol is enhanced by incorporating the limited-view artifacts identification criterion shown in Eq. (6) into the singular value soft-thresholding process as follows. This modified SVT is referred to as a heuristic SVT operation (hSVT):

$$\text{hSVT}_{\lambda, \gamma}(\mathbf{X}) = \mathbf{U}(\mathbf{\Sigma} - \lambda \mathbf{I})_h \mathbf{V}^T, \quad (7)$$

$$[(\mathbf{\Sigma} - \lambda \mathbf{I})_h]_{r, r} = \begin{cases} \sigma_r - \lambda, & r \in \Omega_1 \cap \Omega_2 \\ 0, & \text{otherwise} \end{cases} \quad (8)$$

where,

$$\Omega_1 = \{r \mid \sigma_r \geq \lambda\} \quad (9)$$

$$\Omega_2 = \left\{ r \mid |\mathcal{F}(V_r)|\left(\frac{n}{2t_s}\right) < \gamma |\mathcal{F}(V_r)|_{\max} \right\}. \quad (10)$$

As a result, the proposed eSMART-RECON algorithm is implemented using the following pseudo-code:

```

1:  $k \leftarrow 1$ 
2: while  $\|\vec{\mathbf{X}}^{(k)} - \vec{\mathbf{X}}^{(k-1)}\|_2^2 \geq \epsilon$  do
3:    $\vec{\mathbf{X}}^{(k)} \leftarrow \vec{\mathbf{X}}^{(k-1)} + \delta \mathcal{A}^T \mathcal{D} \left[ \vec{\mathcal{Y}} - \mathcal{A} \vec{\mathbf{X}}^{(k-1)} \right]$ 
4:    $\mathbf{E} \leftarrow \frac{1}{N} \mathbf{1} \mathbf{1}^T \mathbf{X}^{(k)}$ 
5:    $\mathbf{X}^{(k)} \leftarrow \mathbf{X}^{(k)} - \mathbf{E}$ 
6:    $\mathbf{X}^{(k+1)} \leftarrow \text{hSVT}_{\lambda, \gamma}(\mathbf{X}^{(k)})$ 

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7:  $\mathbf{X}^{(k+1)} \leftarrow \mathbf{X}^{(k+1)} + \mathbf{E}$ 
8: end while

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In this pseudocode, $\mathbf{1} \in \mathbb{R}^{N \times 1}$ is a column vector containing all ones and $\mathbf{1}^T$ is its transpose. $\mathbf{E} = \frac{1}{N} \mathbf{1} \mathbf{1}^T \mathbf{X}^{(k)}$ is an image matrix in which each row is filled with the arithmetic average of the column vectors in $\mathbf{X}^{(k)}$. In line 5, the arithmetic average value is subtracted from each image voxel for every column in image matrix $\mathbf{X}^{(k)}$. Line 3 is the gradient descent step of the statistically weighted data fidelity term in Eq. (1). This implementation was inspired by the forward-backward splitting algorithm [26]–[28] with the modified proximal operator shown in Eq. (7). The criterion for identifying temporal bases representing limited-view artifacts, Eq. (6), has been incorporated into the heuristic SVT operation, Eq. (8)–Eq. (10). The heuristic SVT operation forms the essential step in the pseudocode (line 6).

The spatial-temporal image matrix $\mathbf{X}^{(0)}$ was initialized using all the data acquired in each sweep; the statistically weighted data fidelity term without nuclear norm regularizer in Eq. (1) was solved using Landweber iterations [27], [29] with an empirically chosen iteration number (15 in this paper). This procedure allows one to generate T_s image column vectors. These T_s image column vectors were then linearly interpolated along the temporal dimension to generate image columns in all $T = T_s T'$ columns to initialize the image matrix $\mathbf{X}^{(0)}$.

An empirical stopping criterion was used to terminate iteration: by evaluating the change of the cost function with the number of outer and inner loops described in the eSMART-RECON pseudocode, it was found that 10 outer loops ($K = 10$, K denotes the number of outer loops) with 15 inner loops per outer loop yielded empirical convergence of the algorithm with relative change of the cost function, $|\hat{f}^{(k+1)} - \hat{f}^{(k)}| / \hat{f}^{(k)}$, to be less than 10^{-5} , where $\hat{f}^{(k)}$ denotes the cost function value at k -th iteration.

The algorithm was implemented in C using the Compute Unified Device Architecture (CUDA) technology on a local workstation equipped with graphic processing units (GPU) (GTX Titan Z and Quadro P6000, NVIDIA Corporation, Santa Clara, CA).

III. Validation Studies and Quantitative Performance Evaluation of eSMART-RECON: Materials and Methods

The central claim in this paper is that the incorporation of limited-view artifacts criterion Eq. (6) in eSMART-RECON algorithm enables a significant improvement of temporal resolution in TR-CBCT with a multi-sweep CBCT data acquisition protocol. To rigorously validate this claim, the following key technical questions must be addressed with quantifiable metrics:

1. What is the achievable temporal resolution of eSMART-RECON when it is applied to the multi-sweep CBCT data acquisition protocol?
2. How does the performance change when the eSMART-RECON is applied to the clinical multi-sweep TR-CBCT datasets?

To address the first question, ground truth is needed. In this paper, a high temporal resolution fractal tree based vascular structure phantom was used to generate synthetic CBCT projection datasets with known ground truth contrast dynamics of the vasculature. Several quantitative metrics were then used to characterize the trade-off between limited-view artifacts and temporal-average artifacts. These quantitative metrics were used to seek for the optimal parameters including the regularization parameter λ and the number of angular sub-sector T' . To address the second question, the eSMART-RECON with the optimized reconstruction parameters was applied to the *in vivo* human subject data to demonstrate the feasibility of generating high temporal resolution imaging to enable TR-CBCT angiography and cone-beam CT perfusion imaging.

A. Numerical simulation studies: Phantom design and quantitative evaluation metrics

1) Construction of numerical phantom: To generate a human-like vascular tree with sufficiently complex branching pattern yet with ground truth contrast dynamics, a fractal tree¹ model [30] was used to construct the numerical phantom. The phantom is shown in Fig. 2. In this model, a branching vascular network was created starting with a set of feeding arteries, and connecting pattern of vascular network was determined to minimize viscous drag [31]. Temporal contrast enhancement curve of artery and vein are manually selected to mimic a contrast injection protocol in prototype multi-sweep acquisition for cerebral perfusion imaging. A spatial time-of-arrival map was pre-defined for each voxel, such that the temporal curve at each point within the vessels can be generated.

The data acquisition geometry was designed to simulate the scans performed in the human subject study. To be specific, the angular span of the data acquisition was the short-scan angular range with a 20° cone angle (total scan range is 200°). The data acquisition time per sweep was 4.2 seconds plus a 1 second pause. A total of $N_v = 248$ cone beam projections were acquired for each sweep. Of the 10 total simulated sweeps, 8 contrast filled (contrast-enhanced) sweeps cover the temporal span of the contrast uptake curve. Each cone beam projection includes 616×480 measured line integrals. Since the temporal information of the TR-CBCT angiography has been encoded into cone beam projection at each view angle in this multi-sweep data acquisition protocol, the simulated CBCT projection data for the TR-CBCTA phantom were generated numerically using the Siddon method [32]. At each specific time point that corresponds to a specific view angle, the correspondingly enhanced vascular volume was forward projected to generate CBCT projection data for temporal information encoding. This process was repeated for the total of 2480 cone beam projection view angles from 10 sweeps back-and-forth data acquisitions. To simulate a 52 second data acquisition duration, two mask sweeps plus a total of eight filled sweeps (four forward rotations and four backward rotations) were simulated.

Poisson noise was added to the pre-log projection data to simulate the quantum noise in x-ray data acquisitions. The initial photon fluence at each ray was 1×10^5 photons per ray to achieve a noise level similar to that in current clinical prototype multi-sweep acquisition

¹source code available: <https://bitbucket.org/kmjohanson3/mri-fractalphantom>

protocols with IV injection protocols. An image matrix size of $256 \times 256 \times 256$ was used to reconstruct each time frame using an isotropic voxel size of 0.78 mm.

2) Quantitative metrics to quantify image artifacts: To quantitatively assess the performance of SMART-RECON and eSMART-RECON methods in TR-CBCT angiography imaging, metrics are needed for the quantification of temporal-averaging effect and limited-view artifacts level. The severity of temporal-average effect directly impacts the temporal fidelity of the reconstructed TR-CBCT angiographic images. In general, the temporal-averaging effect can be mitigated by reducing the angular span of the data used to reconstruct an individual time frame. However, a reduction of the angular span used to reconstruct the images inevitably exacerbates the associated limited-view artifacts. Therefore, one also needs to quantify the severity of the limited-view artifacts, such that the reconstruction parameters can be appropriately chosen to maximally mitigate both temporal-averaging and limited-view artifacts.

In the reconstructed images, the temporal-average effect mainly impacts the vasculature, while limited-view artifacts appear primarily in the background of the image outside the vascular structures. Therefore, it is advantageous to isolate vascular and non-vascular structures using the known vascular masks M_{angio} and non-vascular mask $M_{\text{bkg}} = \mathbb{I} - M_{\text{angio}}$ in the numerical phantom. Here, $\mathbb{I}$ is an all-one matrix. The entry-wise Hadamard product of the angiography mask M_{angio} , and the reconstructed image was used to isolate temporal-averaging contribution. Similarly, the background was isolated by using the entry-wise Hadamard product of the non-vascular mask M_{bkg} and the reconstructed image.

After the isolation of vascular structure and non-vascular structure in a reconstructed image volume, the temporal-average artifact (TAA) and limited-view artifacts (LVA) can be quantified using the following metrics:

$$\text{TAA} = \frac{\sum_t \|M_{\text{angio}} \circ (X_t - X_{\text{truth},t})\|_2}{\sum_t \|M_{\text{angio}} \circ X_{\text{truth},t}\|_2}, \quad (11)$$

$$\text{LVA} = \frac{\sum_t \|M_{\text{bkg}} \circ (X_t - X_{\text{truth},t})\|_2}{\sum_t \|M_{\text{bkg}} \circ X_{\text{truth},t}\|_2}, \quad (12)$$

where $\circ$ is the Hadamard product. X_t denotes the reconstructed t -th sub-frame image and $X_{\text{truth},t}$ denotes the corresponding ground truth. Each image sub-frame is associated with a given angular sub-sector. Since the central view angle of each sub-sector is known, the ground truth image volume corresponding to the central view angle of each sub-sector is also known and can be used as a reference to quantify the artifacts levels as described in Eqs. 11 and 12.

To quantify the total artifacts level (TAL), these two metrics were combined as follows:

$$\text{TAL} = \sqrt{\text{TAA}^2 + \text{LVA}^2}. \quad (13)$$

The TAL metric was used to optimize the reconstruction parameters as described in the next section.

3) Optimization of reconstruction parameters: TAA, LVA, and TAL depend on the two reconstruction parameters, i.e., the regularization strength λ and the number of sub-sector per sweep T' . To define a common search range of the regularization strength, the largest singular values of the spatial-temporal matrix $\mathbf{X}$ in *the first iteration* was used as the reference value for the regularization parameter. In other words, the regularization strength was represented as $\lambda = x\%$ of σ_1 , where σ_1 is the largest singular value from the spatial-temporal matrix $\mathbf{X}$ in *the first iteration*.

To investigate the dependence of SMART-RECON and eSMART-RECON on λ and T' , each short-scan filled sweep was retrospectively sorted into $T' = \{1, 2, 5, 10, 20, 40, 80, 160\}$ non-overlapping angular sub-sectors, and the regularization strengths were selected as $\lambda = \{100, 10, 1, 0.1, 0.01, 0.001\}$ (% of σ_1). For convenience, we use the nominal frame rate, f_{nom} as a surrogate for the number of sub-sectors per sweep, T' , where $f_{\text{nom}} = \frac{T'}{t_s}$. In the current multi-sweep acquisition protocol, the aforementioned range of T' gives the range of nominal frame rate of $f_{\text{nom}} = \{0.25, 0.5, 1, 2, 4, 8, 16, 32\}$ (fps).

For each given set of reconstruction parameters (λ and f_{nom}), both SMART-RECON and eSMART-RECON were used to reconstruct the spatial-temporal image matrix. As described in section III-A2, TAA, LVA, and TAL were calculated for image matrix corresponding to each set of reconstruction parameters. For the purpose of parameter optimization, it is desirable to generate a relative smooth dependence of the quantitative metric on λ and f_{nom} . Since both λ and f_{nom} can be represented as $\lambda = 10^n$ (% of σ_1), $n = \{-3, -2, -1, 0, 1, 2\}$ and $f_{\text{nom}} = 2^n$ (fps), $n = \{-2, -1, 0, 1, 2, 3, 4, 5\}$, it is natural to convert λ and f_{nom} to log-scale first and then apply a cubic spline interpolation in the domain of $\log_{10} \lambda - \log_2 f_{\text{nom}}$ to generate smooth contour maps (see Fig. 3).

Note that f_{nom} is only determined by the angular span of an individual sub-sector used in limited-view angle reconstruction. However, due to the introduction of regularization, the achievable frame rate $f_{\text{achievable}}$ of a given reconstruction methods may not be as high as the f_{nom} . The nominal frame rate can be considered an upper bound of the achievable frame rate of a given reconstruction method with optimal reconstruction parameters. The actually achievable frame rate can be quantified by the metric introduced in next section. The pair of parameters (f_{nom} , λ) leading to the lowest TAL was selected to be the optimal reconstruction parameters.

4) Quantification of achievable frame rate (i.e., temporal resolution) in

SMART-RECON and eSMART-RECON: For a given ground truth temporal curve, the measured temporal curve from the reconstructed image volumes can be considered as the convolution between the ground truth curve and Gaussian function with a kernel width, σ_w , as shown in [23]. After the optimal width is determined, the achievable frame rate can then be calculated in the following equation.

$$f_{\text{achievable}} = \min \left\{ \frac{1}{2.4\sigma_w}, f_{\text{nom}} \right\}. \quad (14)$$

Note that, as indicated in Eq. (14), the nominal frame rate is the upper bound of achievable frame rate.

B. Validation studies using human subject data sets

To demonstrate the feasibility and robustness of the eSMART-RECON method to human subject cases, two *in vivo* human subject datasets acquired with an IRB approval and written informed consent were retrospectively analyzed to generate high temporal resolution TR-CBCT angiography and cerebral perfusion maps. The multi-sweep CBCT acquisitions were performed using a biplane angiographic system with flat-panel detector (Axiom Artis zee, Siemens Healthineers, Forchheim, Germany). The specific imaging geometry and data acquisition protocol are described in section III-A1. Intravenous contrast injections were performed through the antecubital vein using a dual-syringe power injector. 24 ml of contrast material (370 mg/ml; Omnipaque-300; GE Healthcare; USA) were injected at a rate of 3 ml/s followed by 10 ml of saline chase. During the total data acquisition duration, two mask sweeps plus eight filled sweeps (four forward rotations and four backward rotations) were performed (5 sec and 200° per sweep, 0.5° angular interval, operated at 77 kVp tube potential). The air Kerma rate measured at the reference point (15 cm from iso-center, towards the x-ray tube) is 0.36 μGy per frame. Based on a previous experimental study on the radiation dose of C-arm CBCT [33], the absorbed dose and the effective dose of our multi-sweep acquisition were estimated to be 120 mGy and 5 mSv, respectively. Note that only one tube-detector assembly in the bi-plane data acquisition system has cone-beam CT acquisition capability.

IV. Results

A. Results from numerical simulation studies

1) Optimization of Reconstruction Parameters: The dependence of LVA, TAA and TAL on regularization strength and nominal frame rate of both SMART-RECON and eSMART-RECON were summarized in Fig. 3. As shown in Fig. 3 (a), the LVA of SMART-RECON increases with larger nominal frame rate and smaller regularization strength and vice versa. In contrast, as shown in Fig. 3 (b), the LVA of eSMART-RECON is almost independent of both the nominal frame rate and regularization strength. This property dictates that one can potentially improve temporal resolution by eSMART-RECON without the problem of severe limited-view artifacts.

However, the absence of limited-view artifacts alone does not guarantee an accurate recovery of temporal fidelity in TR-CBCT imaging; one must also check the temporal fidelity as indicated by TAA levels. As shown in Fig. 3 (c) and (d), the TAA of SMART-RECON and eSMART-RECON presents similar dependence on the reconstruction parameters. The TAA monotonically decreases with a decrease of the regularization parameter. However, the TAA does not monotonically depend on the nominal frame rate. In fact, TAA indeed decreases until the frame rate reaches about 7 fps, then it increases with

higher nominal frame rates. Note that when the nominal frame rate increases, the number of projection views per sub-sector decreases. When the number of available CBCT projections is too low, temporal fidelity may not be successfully decoded from data as one can intuitively deduce.

A balance of minimization of both LVA and TAA is achieved via the minimization of TAL, which is used as the figure-of-merit to optimize reconstruction parameters. As indicated by the white dot and white cross in Fig. 3 (e) and (f), the optimal reconstruction parameters of SMART-RECON are $(\tilde{f}_{\text{nom}}, \tilde{\lambda})_{\text{SMART}} = (1.1 \text{ fps}, 0.28\% \text{ of } \sigma_1)$ and optimal reconstruction parameters of eSMART-RECON are $(\tilde{f}_{\text{nom}}, \tilde{\lambda})_{\text{eSMART}} = (7.5 \text{ fps}, 0.01\% \text{ of } \sigma_1)$ respectively.

2) Overall qualitative image quality assessment: A whole brain maximal intensity projection (MIP) was used to generate the corresponding MIP images of the angiograms shown in Fig. 4. The corresponding ground truth MIP images and FBP MIP images were presented in the first and second columns of the figure. Angiograms generated by prior image constrained compressed sensing (PICCS) [19], [20], [34], spatial-temporal total-variation-based statistical image reconstruction (ST-TV-SIR) [35], SMART-RECON, and eSMART-RECON with corresponding optimal reconstruction parameters are shown in the third to sixth columns, respectively. For each individual reconstruction method, the angular range of projection data and reconstruction parameters were empirically optimized for the most appealing reconstruction performance. For example, a densely-sampled short-scan angular range (248 projections acquired within 200°) and Ram-Lak filter were used in FBP reconstruction. As demonstrated in [21], PICCS enables high quality image reconstruction using data acquired from half short-scan angular range (124 projections within 100°). In this paper, $\mu = 2 \times 10^{-5}$, $\lambda = 0.1$, $s = 0.2$, $\alpha = 0.5$, $N_{\text{Iter}} = 15$, and $N_{\text{denoising}} = 100$ were used for PICCS reconstruction. By empirical reconstruction parameter optimization, half short-scan angular range was used in ST-TV-SIR reconstruction. Optimal reconstruction parameters for ST-TV-SIR are $\mu_{\text{spatial}} = 2 \times 10^{-5}$, $\mu_{\text{temporal}} = 1 \times 10^{-5}$, $\lambda = 0.1$, $s = 0.2$, $N_{\text{Iter}} = 15$, and $N_{\text{denoising}} = 100$. The implementation of both PICCS and ST-TV-SIR was based on a generalization of the algorithm for total-variation-based statistical image reconstruction presented in [28]. Reconstruction parameters for SMART-RECON and eSMART-RECON were optimized in section IV-A1.

As demonstrated by Fig. 4, all reconstruction methods generate high quality angiograms without visually noticeable limited-view artifacts. However, the temporal enhancement of the vasculature is more accurate in eSMART-RECON than other methods, particularly for the early time frames (11.8 sec and 13.2 sec).

3) Quantitative Assessment of Temporal Fidelity: Contrast uptake curves were also measured in four pairs of ROIs in four different segments of the vascular tree from the beginning of the arteries to veins. The four ROIs are labelled as (1), (3), (5), (7) in Fig. 2 (a). Since the temporal behaviors of the left and right vessel trees are symmetric in the numerical phantom, only the measured temporal curves from the left vascular tree were presented in Fig. 5. For the distal-end artery (Fig. 5 (c)) and vein (Fig. 5 (d)), both SMART-RECON and eSMART-RECON can reproduce the temporal behavior nearly perfectly. However, other

methods show slightly lower peak enhancement. For middle artery (Fig. 5 (b)), temporal curve measured from FBP, PICCS, ST-TV-SIR, and SMART-RECON angiogram present earlier enhancement for the first several seconds that correspond to fast-varying contrast dynamics. In contrast, temporal curve measured from eSMART-RECON does not show early enhancement, and it matches well with the ground truth curve. For proximal-end artery, temporal curve measured from FBP, PICCS, ST-TV-SIR, and SMART-RECON angiogram present earlier enhancement, lower peak intensity value, and deviates from the ground truth curve. In contrast, due to the higher nominal frame rate provided by eSMART-RECON, temporal curve measured from eSMART-RECON matches the ground truth curve better than SMART-RECON. The lower peak intensity of eSMART-RECON can be partially attributed to the 7.5 fps nominal frame rate is still insufficient to capture the ground truth curve generated at 60 fps frame rate.

4) Quantification of achievable temporal resolution: The achievable frame rates of SMART-RECON and eSMART-RECON were quantified in eight ROIs indicated in Fig. 2 (a). As shown in Fig. 6, for all vessel segments, SMART-RECON provides an achievable frame rate of about 1 fps which has been quantified to be 4.5 times better than that of the conventional FBP reconstruction [23]. For eSMART-RECON, the achievable frame rate is about 4 fps measured at proximal-end artery and about 7.5 fps measured at middle, distal-end artery or vein. As a result, relative to SMART-RECON, eSMART-RECON offers a factor of 4–7.5 times improvement in temporal resolution. When compared with that of the FBP reconstruction, this improvement factor becomes $(4 - 7.5) \times 4.5$, i.e., 18–34 times of improvement in temporal resolution.

Table I summarizes achievable frame rate and total artifacts level using different reconstruction methods. According to the comparison, it has been demonstrated that eSMART-RECON has a factor of 18–34 temporal resolution improvement over conventional FBP reconstruction without any modifications about data acquisition system or protocol. For a given data acquisition protocol, $f_{\text{achievable}}$ of FBP, PICCS, and ST-TVSIR is primarily dominated by the projection angular range for reconstruction (equivalently, f_{nom}). $f_{\text{achievable}}$ of SMART-RECON and eSMART-RECON is bounded by f_{nom} as implied in Eq. (14). Higher reconstruction accuracy (lower TAL value) provided by higher achievable frame rate indicates the need of high temporal resolution in TR-CBCT imaging.

B. Results from the human subject study

With the same optimized parameters, cerebral perfusion maps can be derived from high temporal resolution time-resolved images. Perfusion maps of the 1st human subject are summarized in Fig. 7. Besides SMART-RECON, another state-of-the-art image reconstruction method for perfusion imaging, for example, PICCS and ST-TV-SIR were implemented. The underestimated peak enhancement of arterial input function (AIF) (shown in Fig. 8 (a)) in FBP, PICCS, ST-TV-SIR, and SMART-RECON overestimate the CBF value especially for healthy grey and white matter. The underestimation and inaccurate temporal variation recovery in FBP, PICCS, ST-TV-SIR, and SMART-RECON result in an underestimation of the area of perfusion deficit region. The improved temporal resolution provided by eSMART-RECON captures the temporal variation of cerebral tissues more

accurate as the eSMART-RECON CBF resemble the MDCT CBF qualitatively and quantitatively, while FBP, PICCS, ST-TV-SIR, and SMART-RECON CBF do not.

Even if ischemic core presents in PICCS, ST-TV-SIR, and SMART-RECON CBF, the overestimation of deficit region can not provide an accurate estimation of salvageable tissues, however, eSMART-RECON CBF can discriminate salvageable tissues from ischemic tissues better. Comparing eSMART-RECON CBF and CBV, the location, shape and size of ischemic core can be confirmed, since more symmetric blood volume in CBV implies a collateral supply to the salvageable tissue region. However, using FBP, PICCS, ST-TV-SIR, and SMART-RECON, the discrimination of salvageable and ischemic tissues is not as clear as that using eSMART-RECON.

Fig. 8 shows examples of an AIF and VOF from the human subject dataset reconstructed with different methods for comparison. The higher peak in the eSMART-RECON AIF (see Fig. 8 (a)) improves the temporal fidelity and quantitative accuracy of the perfusion maps (see Fig. 7 for perfusion maps comparison). Results from the 2nd human subject study for the time-resolved CBCT angiography imaging were presented in supplementary material.²

V. Discussion and Conclusion

A. Summary and discussion

In this work, the periodic nature of limited-view artifacts that appear in TR-CBCT images acquired using a multi-sweep acquisition was incorporated into the SMART-RECON framework to enhance its performance in temporal resolution improvement. Extensive numerical studies were performed and validated with two *in vivo* human subject studies to quantify the performance of the proposed eSMART-RECON algorithm. As shown in numerical simulation results, eSMART-RECON enables one to generate 4–7.5 fps temporal resolution in TR-CBCT imaging, despite that fact that it takes about 5 seconds to acquire one short-scan data set per sweep. This represents a factor of 18–34 times improvement in temporal resolution. When compared with the performance of the previous SMART-RECON method, this represents a factor of 4–7.5 times improvement in temporal resolution, since the original SMART-RECON achieves a temporal resolution of 1.0 fps. *In vivo* human subject data were used to demonstrate the feasibility of generating high temporal resolution (4–7.5 fps) TR-CBCT angiography and cerebral perfusion imaging. Note that the results in Fig. 6 demonstrate that the achievable frame rate in eSMART-RECON may depend on the location of vasculature. For proximal arteries, the filling rate of the contrast medium is fast, while the filling rates for distal arteries and veins are much slower. As a result, the achievable frame rate for proximal-end arteries is lower than that for the veins due to the difference in flow rate for these vessels.

Note that in most clinical 2D-DSA protocols, clinicians use frame rates ranging between 4.0 fps to 7.5 fps to guide their interventional procedures and to generate image guidance for interventional procedure planning. However, as discussed in this work, 2D-DSA is limited by the superposition of vessels. In addition, 2D-DSA is typically performed during

²Please see supplemental material for the figure.

interventions with an intra-arterial (IA) contrast injection which is an expensive procedure. With the 4–7.5 fps temporal resolution achieved in TR-CBCT, it is expected that the TR-CBCT angiography and perfusion can be performed in outpatient clinical environment to reduce cost and to provide more accurate delineation of vascular diseases by removing the structure superposition problem in 2D-DSA. When both TR-CBCT angiography and CBCT perfusion imaging are available in interventional suites using the slow gantry rotation C-arm acquisition, the long awaited One-Stop-Shop imaging [17] can be achieved in angiographic suites. To push the developed eSMART-RECON technique toward clinical practice, both data acquisition time and image reconstruction time should be separately discussed and evaluated. In the multi-sweep data acquisition protocol used in this paper, the data acquisition time for the entire perfusion data set is about 1 minute. The image reconstruction time for the tested data sets used in this paper is less than 5 minutes using a state-of-the-art workstation (NVIDIA DGX-1).

B. Limitations and future works

There are several limitations in this work that warrant further investigation. First, clinical evaluations with more human subject data sets are needed to test the robustness of the proposed method. Second, the contrast dynamics in the reconstructed images depend on the contrast injection protocol. The performance dependence of eSMART-RECON based TR-CBCT angiography and perfusion imaging techniques on contrast injection protocol remains unclear. Therefore, the optimization of the contrast injection protocol should be the focus of future work. Third, the performance dependence on inter- and intra-sweep patient motion has not been systematically investigated. In the future, a motion model will be incorporated into eSMART-RECON method to better address patient motion induced inaccuracy.

C. Conclusion

In conclusion, both numerical simulation studies and *in vivo* human subject studies performed in this paper demonstrate that using eSMART-RECON, the temporal resolution of multi-sweep CBCT imaging can be improved to achieve 4–7.5 fps temporal resolution. Compared with the previous SMART-RECON, eSMART-RECON further improve temporal resolution by a factor of 4–7.5, and a factor of 18–34 when it is compared with that offered by the conventional FBP reconstruction. With the proposed eSMART-RECON, the improvement in temporal resolution in the slow gantry rotation C-arm acquisition system enables both accurate TR-CBCT angiography and perfusion imaging in interventional suites.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Fig. 1.

Illustration of SVD of the spatial-temporal image matrix. The images in the first row are different columns of the spatial-temporal image matrix reconstructed from a simple least squared-based reconstruction. The SVD is used to decompose the image matrix ($\mathbf{X}$) into three matrices, $\mathbf{U}$, $\mathbf{\Sigma}$, $\mathbf{V}^T$. The images in the second and third rows correspond to the columns of matrix $\mathbf{U}$ and $\mathbf{V}$ respectively. The images in the last rows are the DFTs of each temporal basis function. Subscript denotes the column index. Images in the first row were displayed with a W/L of 600/0 HU. Bases V_2 , V_6 , V_7 , V_8 are identified as bases to primarily represent limited-view artifacts, since they have peak amplitudes (indicated with red lines) at the following characteristic frequencies, $\pm 1/2t_s, \pm 6/2t_s, \pm 3/2t_s, \pm 6/2t_s (s^{-1})$, respectively.

Fig. 2. Illustration of the TR-CBCTA phantom. (a) coronal maximal intensity projection (MIP) image and (b) sagittal MIP image. Selected region-of-interest (ROI) to measure temporal curves and to quantify achievable frame rate: (1)–(2) proximal-end artery; (3)–(4): middle artery; (5)–(6): distal-end artery; and (7)–(8): vein.

Fig. 3. Optimization of reconstruction parameters. The dependence of the LVA ((a) and (b)), the TAA ((c) and (d)), and the TAL ((e) and (f)), with respect to the nominal frame rate and relative regularization strength for both SMART-RECON and eSMART-RECON respectively. Note that λ and f_{nom} were first converted to log-scale and a cubic spline interpolation was applied in the domain of $\log_{10} \lambda - \log_2 f_{nom}$ to generate smooth contour maps shown in this figure.

Fig. 4.

Coronal MIP images generated from ground truth, FBP, PICCS, ST-TV-SIR, SMART-RECON, and eSMART-RECON. Images are displayed with W/L: 300/150 HU. The total artifact level (TAL, defined in Eq. (13)) for each of these images were calculated.

Fig. 5.
Temporal curves of different reconstruction methods measured at four ROIs ((1), (3), (5), (7) in Fig. 2 (a)).

Fig. 6. Achievable frame rate of SMART-RECON and eSMART-RECON quantified at eight ROIs shown in Fig. 2 (a).

Fig. 7. Qualitative assessment of perfusion maps of a human subject before endovascular treatment. For same type of perfusion map, same display window are used. Display windows are shown in the last column.

Fig. 8. Temporal curves of different reconstruction methods measured at artery and vein of the human subject.

TABLE I

Achievable frame rate ($f_{\text{achievable}}$) and total artifacts level (TAL) for different reconstruction methods.

Reconstruction method	Achievable frame rate (fps)	TAL (%)
FBP	0.2	36.5
PICCS	0.4	24.1
ST-TV-SIR	0.4	23.7
SMART-RECON	1	15.8
eSMART-RECON	4–7.5	6.3