Dynamic cone beam CT angiography of carotid and cerebral arteries using canine model

Weixing Cai

Department of Imaging Sciences, University of Rochester, 601 Elmwood Avenue, Rochester, New York 14642

Binghui Zhao^{b)}

Department of Radiology, Shanghai 6th People's Hospital, 600 Yishan Road, Xuhui, Shanghai, China

David Conover

Koning Corporation, Lennox Tech Enterprise Center, 150 Lucius Gordon Drive Suite #112, West Henrietta, New York 14586

Jiangkun Liu

Department of Imaging Sciences, University of Rochester, 601 Elmwood Avenue, Rochester, New York 14642

Ruola Ning^{a)}

Department of Imaging Sciences, University of Rochester, 601 Elmwood Avenue, Rochester, New York 14642 and Koning Corporation, Lennox Tech Enterprise Center, 150 Lucius Gordon Drive Suite #112, West Henrietta, New York 14586

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Purpose: This research is designed to develop and evaluate a flat-panel detector-based dynamic cone beam CT system for dynamic angiography imaging, which is able to provide both dynamic functional information and dynamic anatomic information from one multirevolution cone beam CT scan.

Methods: A dynamic cone beam CT scan acquired projections over four revolutions within a time window of 40 s after contrast agent injection through a femoral vein to cover the entire wash-in and wash-out phases. A dynamic cone beam CT reconstruction algorithm was utilized and a novel recovery method was developed to correct the time-enhancement curve of contrast flow. From the same data set, both projection-based subtraction and reconstruction-based subtraction approaches were utilized and compared to remove the background tissues and visualize the 3D vascular structure to provide the dynamic anatomic information.

Results: Through computer simulations, the new recovery algorithm for dynamic time-enhancement curves was optimized and showed excellent accuracy to recover the actual contrast flow. Canine model experiments also indicated that the recovered time-enhancement curves from dynamic cone beam CT imaging agreed well with that of an IV-digital subtraction angiography (DSA) study. The dynamic vascular structures reconstructed using both projection-based subtraction and reconstruction-based subtraction were almost identical as the differences between them were comparable to the background noise level. At the enhancement peak, all the major carotid and cerebral arteries and the Circle of Willis could be clearly observed.

Conclusions: The proposed dynamic cone beam CT approach can accurately recover the actual contrast flow, and dynamic anatomic imaging can be obtained with high isotropic 3D resolution. This approach is promising for diagnosis and treatment planning of vascular diseases and strokes. © 2012 American Association of Physicists in Medicine. [DOI: 10.1118/1.3673068]

Key words: cone beam CT, angiography, dynamic imaging

I. INTRODUCTION

Flat-panel detector-based (FPD-based) cone beam CT (CBCT) technique¹ has been developed to address the limitation of conventional multislice CT scanners. Major advantages of CBCT include larger volume coverage, faster volume data acquisition, three-dimensional isotropic resolution, better dose efficiency, and flexibility in specific applications. The CBCT technology has become a great success in many applications, including breast imaging,^{2,3} cardiac imaging,^{4,5} dental imaging,⁶ image-guided therapy,⁷⁻⁹ and small

animal imaging.^{10,11} CBCT has also been used for vascular imaging with contrast injection.^{12,13} In all these applications, however, the CBCT has imaged the anatomy of organs only, and high-resolution full-coverage functional imaging is still in its infancy stage and remains a challenge.

The idea of the dynamic cone beam CT (dynamic CBCT) technique has been proposed in previous literatures.¹⁴⁻¹⁶ As that for conventional dynamic CT, there are two potential clinical applications for dynamic CBCT: angiogenesis imaging and perfusion imaging.¹⁷ As angiogenesis is critical for tumor growth, progression, and metastasis, it is possible to

characterize a tumor by imaging its contrast kinetics.^{18–21} For the purpose of diagnosis and treatment of ischemic stroke,²² dynamic CBCT can also be used to obtain a 3D perfusion map of ischemic brain tissues and to find the reason of stroke (stenosis, for example) by imaging anatomic and functional information of carotid and cerebral arteries. The fundamentals of both applications involve imaging and measurement of the time-enhancement curve of contrast flow in arteries, tissues, or veins.

Dynamic cone beam CT has been successfully implemented in our laboratory using mouse models for tumor angiogenesis studies.¹⁵ A mammary tumor was grown in the mouse and the dynamic imaging technique was successfully implemented to investigate the time-enhancement curves to characterize tumor angiogenesis and malignancy.¹⁵ However, a major limitation of this research is that the measured time-enhancement curve is not the actual trend of contrast flow because the procedure of sequential reconstructions averages the contrast agent intensity over each reconstruction interval. This reduces contrast enhancement and deforms the time-enhancement curve compared to the actual dynamics. There is a necessity to recover the actual time-enhancement curve that should show better enhancement and more accurate dynamic features. This is especially important for the potential of cone beam CT perfusion imaging where much higher temporal resolution (<1 s) and contrast resolution (<20 HU) are required.

Several other research groups have published valuable results in dynamic CT imaging as well. Grangeat *et al.*²³ developed a dynamic particle model and presented a framework to reduce motion artifact in the reconstruction of a dynamic multislice CT scan. Similarly, Montes *et al.*²⁴ adopted an interpolation method on projection data to reduce the motion artifact in dynamic reconstruction in perfusion CT. Nett *et al.*²⁵ developed a compressed sensing-based iterative algorithm to accurately reconstruct the enhancement of tissues using the nonenhanced anatomy as prior knowledge. These works improved the reconstruction accuracy of dynamic imaging. Neukirchen *et al.*²⁶ presented an iterative approach that utilized a decomposition model to recover the real trend of time-enhancement curves. All the previous works were performed using either a regular multislice CT or a micro-CT, and none of them have been applied to a flat-panel detector-based CBCT system. In our research, reconstruction accuracy is not a concern since no obvious motion artifact was observed, while the inaccuracy of the time-enhancement curve due to the slow-rotation of the CBCT gantry is a problem in characterizing contrast flow, which will be treated using a deconvolution approach in this work.

There is also a clinical demand that both anatomic and functional information are obtained through a single imaging procedure.²⁷ Currently, standard clinical procedures for anatomic vascular imaging include digital subtraction angiography (DSA) and CT angiography (CTA), while CT perfusion (CTP) is the standard procedure for functional imaging of tissues and vessels. DSA and CTA show higher resolution for anatomy structure (typical 0.1 mm for DSA and 0.6 mm for CTA using helical CT), but they cannot provide dynamic

information. On the contrary, CTP is able to show dynamic information with a much lower spatial resolution (5–10 mm longitudinal resolution), and therefore, it cannot provide adequate details of anatomy. Patients are routinely required to take separate procedures to obtain both anatomic and functional information, which brings additional exposure dose and anxiety to patients. In addition, CTA and CTP are generally associated with a limited longitudinal coverage (~ 4 cm for a 64 slice CT scanner) and their spatial resolution is nonisotropic and lower compared to CBCT. Although the emerging 320-slice CT scanner has greatly expanded the longitudinal coverage as comparable to that of a CBCT scanner (~ 20 cm longitudinally), CBCT is able to provide an isotropic spatial resolution that is twice as high as the 320-slice CT. The imaging chain with a flat-panel detector can be flexibly adapted to investigate the dynamics of specific organs, like contrast-enhanced breast imaging. Therefore, the dynamic CBCT technology can potentially combine the advantages of both CTA and CTP, which is expected to efficiently obtain and present both anatomic and functional information of organs with an isotropic high spatial resolution and a large coverage.

This study demonstrates dynamic cone beam CT imaging of the carotid and cerebral arteries using the canine model. Both the functional and anatomic information of the carotid and cerebral arteries have been investigated and validated in a dynamic imaging scheme. Major contributions of this work include: (a) a new recovery method is proposed to correct the time-enhancement curve of contrast flow to improve contrast and accuracy; (b) by using the flat-panel detector-based dynamic cone beam CT, both anatomic and functional features of vessels were obtained with high isotropic resolution through a single multirevolution scan. (c) the anatomic information of the vascular structure is presented in a dynamic way using either projection-based subtraction prior to reconstruction or reconstruction-based subtraction; (d) dog models were used that have a carotid artery system of similar size and anatomy as that of humans.

The paper is organized as follows: Section II will describe the dynamic cone beam CT system designed and built in our laboratory, issues with dynamic functional imaging and issues with dynamic anatomy imaging. Section III will present the simulation results of the novel recovery approach and experimental results of dog studies, and Sec. IV will conclude this research.

II. METHODS AND MATERIALS

II.A. The dynamic cone beam CT system

A prototype system was designed and built in our laboratory for dynamic cone beam CT studies.¹⁴ It consisted of a CT gantry (modified HiSpeed Advantage, GE Medical System, Milwaukee, WI) with an angiography x-ray tube (G1593BI, Varian X-ray Products, Salt Lake City, UT), a flat-panel detector (PaxScan 4030CB, Varian Imaging Products, Salt Lake City, UT) and an x-ray generator (SHF635ROCH-480VAC, Sedecal USA, Arlington Heights, IL) mounted on the gantry, and a CT table and. A console computer controlled

FIG. 1. A photo of the dynamic cone beam CT angiography system.

the gantry rotation, x-ray triggering and encoder readout of the gantry angle position, and an on-board computer controlled real-time (30 fps) image acquisition through an internal frame grabber (Roadrunner, Bitflow Inc., Woburn, MA). To enforce continuous CBCT scans for dynamic imaging, slip ring technology was incorporated into this system for transferring electrical power and control signals. Image data were temporarily stored on the on-board computer during the scan and was transferred to the off-board reconstruction computer after the scan. Figure 1 is a photograph of the prototype system and the experiment parameters are shown in Table I.

For this study, the system was operated at 120 kVp and 40 mA. The x-ray triggers were synchronized with the frame grabber at 30 fps and the pulse width was set as 6 ms. The gantry rotation speed was 6 rev/min, or 10 s per revolution. The angular interval was 1.2 and the total projection number for a dynamic CBCT scan was 1200. Current hardware and software configurations allowed a maximum of four revolutions per dynamic scan. The exposure level was about 3.5 mR per frame measured at the rotation axis using an air chamber, and the total absorbed dose by the dog was estimated around 40 mGy for a complete dynamic CBCT scan.

TABLE I. System parameters of the dynamic cone beam CT scanner.

Tube voltage	120 kVp
Tube current	40 mA
Focal spot size	0.3 mm
Pulse width range	6 ms @ 30 Hz
Flat-panel detector (FPD)	PaxScan 4030CB
FPD active area size	397 × 298 mm
FPD pixel pitch	0.388 mm (2 × 2 binning)
FPD frame rate	30 frames/s (2 × 2 binning)
Magnification ($M = \text{SOD}/\text{SID}$)	1.59
Voxel size (isotropic spatial resolution)	(0.244 mm) ³
Number of projection images/revolution	300
Gantry rotation speed	10 s/rev
Maximum revolution number/scan	4
Maximum projection number/scan	1200
Exposure level	~3.5 mR/frame
Estimated dose level	~40 mGy/dynamic scan

II.B. Preparation of the dog

Mongrel dogs of mass 22–24 kg were used in this study as this species offers a vascular system comparable in size to humans. The imaging protocol was approved by the University of Rochester's University Committee on Animal Resources (UCAR). Each dog was fasted 12–16 h before the experiment, and then, it received medetomidine (MI) 0.01 mg/kg as premedication in order to facilitate IV catheter placement. Once the IV catheter was placed, a half-dose of the induction agents were administered (ketamine 10 mg/kg + Diazepam 0.5mg/kg mixed in the same syringe). The dog was then intubated and maintained on isoflurane gas anesthesia during the imaging procedure. After imaging was completed, the dog received one dose of atipamezole to reverse the medetomidine and facilitate recovery as needed. The dog was monitored by a UCAR technician at least every 10–15 min during imaging procedure and parameters monitored included heart rate, respiratory rate, mucous membrane color and pulse oximetry.

The dog was placed on the patient table of our dynamic cone beam CT system, and its neck and head were positioned using a U-shaped plastic holder. Optiray 350 contrast agent was injected through an IV catheter using a power injector. Consistent with clinical standards, the injection pressure was set at 750 psi, total dose of contrast agent was set at 30 ml (~1.3 ml/kg) and the injection rate was set at 3 ml/s.

II.C. Dynamic functional imaging

The principle of dynamic cone beam CT imaging has been introduced,^{15,16} where half-scan reconstruction and full-scan reconstruction have been proposed. In this section, the principle is reviewed and generalized.

Figure 2 illustrates the principle of dynamic cone beam CT imaging. The curve $f(t)$ shows the true time-enhancement curve of the volume-of-interest (VOI) such as vessels or tissues due to contrast flow. Assumptions include that the cone beam CT system gantry continuously rotates and acquires

FIG. 2. Illustration of dynamic cone beam CT functional imaging. $f(t)$ is the true time-enhancement dynamic trend while $g(t)$ is the measured curve.

projection images at a constant frame rate and rotation speed, and total rotation time is T . It doesn't matter if T is an integer multiple of the duration of a single revolution. Then, a set of reconstructions was computed in a way such that the first projection for each reconstruction is selected at a time sequence $t_1, t_2, t_3, \dots, t_N$ and the projection data used for each reconstruction were selected corresponding to a time interval of Δt . The enhancement values were then measured at the VOI from the set of reconstructions, and the measurements were plotted versus time to characterize the functional feature of VOI, which is shown as curve $g(t)$.

It should be noted that $g(t)$ is not exactly $f(t)$ because each measurement on $g(t)$ is actually the time average of $f(t)$ over a period of Δt , given that the projections are nearly equally weighted in the reconstruction procedure. Compared to the features in the real trend $f(t)$, curve $g(t)$ has an earlier and steeper uptake but lower maximum enhancement. To recover $f(t)$ from $g(t)$, a recovery algorithm is presented in the following paragraphs.

We assume the actual "real-time" enhancement $f(t)$ is differentiable to the first order, which is true for an actual contrast enhancement curve due to constant blood flow. As shown in Fig. 3, the maximum enhancement occurs at the moment t_0 where

$$f'(t)|_{t=t_0} = 0. \quad (1)$$

A "cumulative function" of $f(t)$ is defined as

$$F(t) = \int_{-\infty}^t f(t') dt', \quad (2)$$

and clearly

$$\frac{dF(t)}{dt} = f(t). \quad (3)$$

As $g(t)$ can be considered as the time average of $f(t)$ over the interval Δt , $g(t)$ is expressed as

$$g(t) = \frac{1}{\Delta t} \int_t^{t+\Delta t} f(t') dt' = \frac{F(t + \Delta t) - F(t)}{\Delta t}. \quad (4)$$

FIG. 3. Relationship between curves $f(t)$ and $g(t)$.

Clearly $g(t)$ is also differentiable for the first order. The maximum enhancement of $g(t)$ occurs when

$$\frac{dg(t)}{dt} \Big|_{t=t_1} = 0, \quad (5)$$

or

$$\frac{dF(t + \Delta t)}{dt} \Big|_{t=t_1} - \frac{dF(t)}{dt} \Big|_{t=t_1} = f(t_1 + \Delta t) - f(t_1) = 0. \quad (6)$$

That is to say, $t_1 < t_0 < t_1 + \Delta t$. t_1 , the moment of maximum enhancement of $g(t)$, is located before t_0 . If the curve around the peak is roughly symmetric, t_1 is about $\Delta t/2$ before t_0 . It is already known from Eq. (4) that

$$\frac{dg(t)}{dt} = \frac{1}{\Delta t} (f(t + \Delta t) - f(t)). \quad (7)$$

Taking the Fourier transform of both sides, we obtain

$$FT \left\{ \frac{dg(t)}{dt} \right\} = \frac{1}{\Delta t} FT \{ f(t) \} \cdot \{ \exp(j2\pi\Delta t\xi) - 1 \}, \quad (8)$$

where Δ is the reciprocal variable of t in Fourier domain. Then, $f(t)$ can be solved as

$$\begin{aligned} f(t) &= FT^{-1} \left\{ \frac{\Delta t \cdot FT \left\{ \frac{dg(t)}{dt} \right\}}{\exp(j2\pi\Delta t\xi) - 1} \right\} \\ &= FT^{-1} \left\{ FT \{ g(t) \} \frac{j2\pi\Delta t\xi}{\exp(j2\pi\Delta t\xi) - 1} \right\}. \end{aligned} \quad (9)$$

The solution is in the form of a filtration with several poles determined by Δt , and hence, there is a concern of stability in algorithm implementation especially when noise is present. Owing to the fact that a time-enhancement curve is mainly composed of low frequency harmonics,²⁶ the signal and noise can be well separated using regular noise reduction algorithms. In our implementation, a spline fitting is first applied to smooth the raw measurements. To further suppress possible high-frequency vibrations, the signal is up-sampled using spline interpolation to include a larger sample number, and a cosine window, as shown in Eq. (10), is combined with the kernel in Eq. (9) for filtration. The flowchart of the entire implementation can be illustrated in Fig. 4

$$W(f) = \begin{cases} \frac{1}{2} \left(1 + \cos \left(\pi \frac{f}{f_{cutoff}} \right) \right) & f \leq f_{cutoff} \\ 0 & f > f_{cutoff} \end{cases}. \quad (10)$$

FIG. 4. Flowchart of algorithm implementation.

FIG. 5. Illustration of dynamic cone beam CT anatomic imaging.

II.D. Dynamic anatomic imaging

The proposed dynamic cone beam CT approach is able to obtain detailed 3D images of vascular structures at various stages of contrast flows. To highlight the vascular structures, a subtraction method is performed in the reconstruction process to remove background tissues and bones. As shown in Fig. 5, an appropriate delay time was applied at the beginning of the scan such that there is no enhancement in Zone 0, which was referred as the baseline. The projection data from any Zone i that covers the desired stage were processed to obtain the 3D MIP using either volume-based subtraction or projection-based subtraction. Typically, Zone i can be an uptake phase, the peak of enhancement, or a wash-out phase.

As shown in Fig. 6(a), volume-based subtraction is quite straight forward. The 3D vascular structure can be obtained by subtracting the reconstruction of Zone 0 from that of Zone i . The advantage of the volume-based subtraction is that if there is a rigid motion of the object during the scan, it is pos-

sible to obtain a good subtraction by applying registration algorithms. In addition, the location of a Zone i can be arbitrarily selected. However, there is a concern that if there are severe artifacts in the reconstruction, the information of vessels that interferes with the artifact volume might be lost. As our dynamic CBCT system takes projections at a fairly low angular sampling rate of 1.2 per frame, the FDK algorithm may bring streaking artifacts to the reconstruction, especially around high contrast bones. In addition, a large portion of the carotid and cerebral arteries winds along and goes through the bones, which is vulnerable to the artifacts and might be eliminated during volume subtraction. To mitigate this problem, a high x-ray technique was used throughout this study and the modified Shepp-Logan filter was employed in FDK algorithm. We also compared the results from both volume-based subtraction and projection-based subtraction to evaluate the reconstruction accuracy. Projection-based subtraction is shown in Fig. 6(b). It is valid only when corresponding view angles of projections can be found in both Zone 0 and Zone i . It is not necessary that the view angles are sequentially matched. For example, if Zone 0 covers $0^\circ - 360^\circ$ and a Zone i covers $540^\circ - 900^\circ$, the view angles are still matched because the range $0^\circ - 180^\circ$ matches $720^\circ - 900^\circ$ and the range $180^\circ - 360^\circ$ matches $540^\circ - 720^\circ$. The major advantage of projection-based subtraction is that subtle information of vessels may survive because the objects that may cause artifacts (like bones) are cancelled out during subtraction. 3D reconstruction is then performed on the subtracted projections.

II.E. Intravenous DSA

Intravenous DSA was performed to acquire the “actual” time-enhancement curve as a baseline in dog studies. The contrast injection protocol is the same as that of the dynamic cone beam CT scan. At the moment when injection started,

FIG. 6. Reconstruction of the 3D MIP of vessels: (a) volume-based subtraction and (b) projection-based subtraction.

FIG. 7. Simulation results to validate the dynamic CBCT recovery algorithm that recovers the measured time-enhancement curve using (a) full-scan reconstruction and (b) half-scan reconstruction.

the x-ray system started exposures and the flat-panel detector started acquiring a sequence of projection images for duration of T . The nonenhanced projection data from the first several seconds were averaged to reduce noise and used as

the baseline, which was then subtracted from all the sequential projections. In this way, a sequence of 2D vessel images was obtained that was used to find the “actual” information of contrast flow.

FIG. 8. Simulation results with the presence of noise. (a) and (b) show full-scan reconstruction results and (c) and (d) show half-scan reconstruction results. The cutoff frequencies for (a)–(d) are $\pi/8$, $\pi/64$, $\pi/2$, and $\pi/32$, respectively.

FIG. 9. Error analysis for cutoff frequency of the cosine window.

III. RESULTS

III.A. Validation of the dynamic cone beam CT recovery algorithm by simulation

The accuracy of the recovery algorithm was validated through a computer simulation based on the parameters listed in Sec. II A. The phantom is composed of one vessel with defined contrast change with time. A set of reconstructions were computed in a way such that the first projection for each reconstruction is 0.5 s (15 projections) apart. The

noise-free results are shown in Fig. 7, including the full-scan case [Fig. 7(a)] and the half-scan case [Fig. 7(b)]. In both figures the measured curves (black dotted) show earlier uptake of the contrast, earlier occurrence of the peak, reduced contrast (peak value) and distorted curvatures. The recovered curves (dashed) are almost identical to the actual enhancement curves (solid), showing an excellent accuracy of the proposed algorithm. Typical results with the presence of noise are shown in Fig. 8 with different scenarios. Figures 8(a) and 8(b) show the full-scan cases while Figs. 8(c) and 8(d) show the half-scan cases. The numerical cutoff frequencies for (a)–(d) are $\pi/8$, $\pi/64$, $\pi/2$, and $\pi/32$, respectively. Although noise distorted the trends of curves and thus degraded the recovered curves, the recovered curves still agree well with actual curves.

The optimized cutoff frequency was found by calculating the deviation between the actual curve and the recovered curve, defined as

$$Dev = \sqrt{\sum (curve_{actual} - curve_{corrected})^2}. \quad (11)$$

Because of poles in the filtration kernel, the recovery is not stable for high cutoff frequencies. The recovery for the half-scan case is stable within a numerical spectrum up to $\pi/2$, while the full-scan cases is stable only under $\pi/4$. The

FIG. 10. Measurement of the intravenous DSA curve. (a) and (b) show the time-enhancement curves at the fork of the left CCA and the right CCA, respectively. Inserts (i)–(iv) show the IV DSA image of the carotid and cerebral arteries at different stages as marked in (a) and (b). The white blocks indicate the locations of measurements.

deviations were calculated for various cutoff frequencies with which the recovery is stable, and the results are shown in Fig. 9. The deviation is minimized around 0.015π – 0.04π for full-scan case and around 0.03π – 0.07π for half-scan case. In our experimental data processing, a cutoff frequency of 0.03125π ($\pi/32$) was selected for full-scan and 0.0625π ($\pi/16$) was selected for half-scan.

III.B. Intravenous DSA imaging to identify the actual time-enhancement curve

Figures 10(a) and 10(b) show the time-enhancement curves at the fork of the left common carotid artery (CCA) and the right CCA at different stages, respectively. The blue dots are measured points and the solid curves are the fitted trend. Typical IV-DSA images are shown in inserts (i) non-enhancement, (ii) wash-in, (iii) peak, and (iv) wash-out phases.

III.C. Dynamic functional imaging of major carotid arteries

The dynamics of contrast flow was investigated at the fork of each CCA where the common carotid artery becomes an internal carotid artery (ICA) and an external carotid artery (ECA). Based on the IV-DSA curve, a 5 s delay was selected such that there was no enhancement during the first 10 s and the complete 40-s dynamic CBCT scan could cover the entire procedure including nonenhancement, wash-in, and wash-out phases of contrast flow. Both half-scan reconstruction and full-scan reconstruction were applied to perform the dynamic CBCT reconstruction. In the volume reconstruction, the locations of the forks on the left CCA and the right CCA were identified and the averaged CT number at each fork was measured within a volume of $6 \times 6 \times 6$ pixels. The time-enhancement curves were then generated, and the recovered

FIG. 11. Dynamics of contrast flow at the forks of the left CCA [images (a) and (c)] and the right CCA [images (b) and (d)]. (a) and (b) show dynamic CBCT results using full-scan reconstruction while (c) and (d) show the dynamic CBCT results using the half-scan reconstruction. The dotted curves are the original measurements from dynamic CBCT results, the dashed curves are the corrected time-enhancement curve using the proposed recovery algorithm and the solid curves are the fitted curve using IV-DSA measurements, which are considered as the “actual” curve. Images (e)–(h) show typical axial slices where the measurements were taken: (e) non-enhancement stage, (f) wash-in stage, (g) enhancement peak, and (h) wash-out stage.

curves were computed using the proposed recovery algorithm. The curves were then compared with the time-enhancement curve of the IV-DSA experiments at the same location, which is regarded as the “actual” curve of contrast flow. It should be noted that the unit of enhancement in IV-DSA is ADU (analog-to-digital unit) given by the flat-panel detector while the unit of enhancement in dynamic CBCT is CT number (or HU). For a fair comparison, the curve of IV-DSA is scaled by a constant such that the scaled peak value is the same as that of the dynamic CBCT curves. The results are shown in Fig. 11, where (a) and (c) show the dynamics at the fork of the left CCA while (b) and (d) show that of the right CCA. Full-scan reconstruction was performed for (a) and (b) while half-scan reconstruction was performed for (c) and (d). The black dotted curves are the original measurements from dynamic CBCT reconstructions, the dashed curves are the corrected time-enhancement curve using the proposed recovery algorithm and the solid curves are the fitted curve using IV-DSA measurements, serving as the “actual” curve for comparison. The recovered curves resemble the IV-DSA curves very well from the wash-in stage to the wash-out stage, where both time shift and lower contrast were corrected. Images (e)–(h) show typical axial slices where the measurements were taken, including stages of (e) nonenhancement, (f) wash-in, (g) enhancement peak, and (h) wash-out. The change of CT numbers in the cross section of the vessels can be clearly observed.

III.D. Dynamic anatomy imaging of carotid and cerebral arteries

The dynamic anatomy images of the carotid and cerebral arteries were computed using both project-based subtraction and reconstruction-based subtraction. A quantitative comparison of three typical reconstructions is listed in Table II using relative reconstruction error (RRE), which is defined in Eq. (12)

$$\text{RRE} = \frac{\sum_{i,j,k} |T_{ps}(i,j,k) - T_{rs}(i,j,k)|}{\sum_{i,j,k} \frac{|T_{ps}(i,j,k) + T_{rs}(i,j,k)|}{2}}, \quad (12)$$

where T_{ps} and T_{rs} are 3D reconstructions using projection-based subtraction and reconstruction-based subtraction, respectively, and i, j , and k are the three indices of a 3D matrix.

Given that the typical noise level in the background tissue is around 20 HU, the calculated relative reconstruction errors are equivalent to the noise levels at all reconstruction time ranges, and in fact, their 3D volume images of the vascular structure are almost identical. Typical images are shown in Fig. 12 that represents the wash-in (a), peak (b) and washout (c) stages, and (d) illustrates the reconstruction windows of (a)–(c) on a time-enhancement curve. In the wash-in stage the major vessels start to show up. At the peak, the entire vasculature of carotid and cerebral arteries are clearly seen. The

FIG. 12. Dynamic CBCT reconstruction of the carotid and cerebral vascular structure: (a) wash-in phase, (b) peak, and (c) wash-out phase. (d) illustrates the reconstruction windows of (a)–(c) on a time-enhancement curve. Circle of Willis [marked in the circle in (b)] can be clearly observed at the peak phase.

TABLE II. Comparison of the reconstructions using projection-based subtraction and reconstruction-based subtraction.

Reconstruction time range	Relative reconstruction error(%)
10th s–20th s (wash-in)	3.94
15th s–25th s (peak)	3.35
30th s–40th s (wash-out)	4.78

Circle of Willis is highlighted by the red circle, where vessels have a diameter around 1 mm or less. In the washout stage the arteries fade away and the veins start to show up. The bones didn't cause obvious artifacts in the vascular structure.

IV. DISCUSSION AND CONCLUSIONS

Flat-panel detector-based cone beam CT has been used for anatomy imaging for over a decade but the application in dynamic imaging remains a challenge. Recent development of high power, small focal spot x-ray tubes and high resolution flat-panel detectors has facilitated fast image acquisition and thus made dynamic imaging possible. This research presented a dynamic cone beam CT angiography study to image the carotid and cerebral arteries of dogs, which is potentially very useful for the research of vascular diseases (stenosis, aneurysm, atherosclerotic plaques, etc.) and stroke studies of humans. Specifically, this study presented an approach that can obtain both dynamic functional information and dynamic anatomy information from a single multirevolution cone beam CT scan.

The dynamic functional imaging concerns the accuracy of time-enhancement measurements. As a dynamic cone beam CT system generally rotates much slower than a multislice CT, the time-enhancement curve obtained from dynamic reconstructions is the time average of the actual contrast flow, resulting in distorted dynamic feature. This study presented a deconvolution approach to recover the actual dynamics of contrast flow from the measured time-enhancement curve. The computer simulation of the recovery algorithm showed an excellent agreement among the actual contrast flow and the recovered curve from the time-enhancement curve measured using dynamic cone beam CT reconstructions. The experimental results also showed a very good agreement of the recovered curve and the curve measured by IV-DSA. It should be noted that this approach assumes all projections being equally weighted in computing reconstructions, which is valid for the FDK algorithm used through this research. However, if a nonlinear algorithm is employed for reconstruction, each projection may have different weight and the recovered curve is correct up to a weighting function. The weighting function should be estimated from the specific nonlinear reconstruction process. Please see Appendix for more information.

The dynamic anatomy images of the carotid and cerebral arteries were obtained from the same dynamic cone beam CT scan. Both projection-based subtraction method and reconstruction-based subtraction method were tested and they are almost identical, indicating that the possible artifacts around bones did not impact the imaging of arteries.

Typical 3D vascular structures with high isotropic resolution were shown to represent the wash-in, peak, and wash-out phases. The Circle of Willis was clearly seen, indicating that vessels as small as 1 mm in diameter are distinguishable.

Our future studies will include perfusion imaging and imaging guidance procedures using the dynamic cone beam CT technology. With the novel recovery algorithm, it is possible to perform perfusion studies based on the recovered actual dynamics. In addition, a dynamic cone beam CT system is ideal for treatment planning using a stent or balloon catheter because the flat-panel detector can work in a real-time “fluoro” mode for the guidance of catheterization. The functions of diagnosis and treatment guidance can be integrated into a single dynamic cone beam CT angiography unit.

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APPENDIX: CURVE RECOVERY FOR GENERAL RECONSTRUCTION ALGORITHMS

Assume in the reconstruction process each projection is weighted by a normalized factor $w(t)$ that depends on the projection index and thus the time t . Then, the measured curve $g(t)$ is expressed as

$$g(t) = \frac{1}{\Delta t} \int_t^{t+\Delta t} f(t')w(t')dt' = \frac{1}{\Delta t} \int_t^{t+\Delta t} \tilde{f}(t')dt', \quad (\text{A1})$$

where a new function $\tilde{f}(t)$ is defined as the product of $f(t)$ and $w(t)$. It is then straightforward to solve $\tilde{f}(t)$ using the approach described in this manuscript, and the actual curve $f(t)$ can be simply calculated by dividing the weighting function $w(t)$ from $\tilde{f}(t)$. The weighting function $w(t)$ is algorithm-specified and it is not possible to give a general form here. However, as long as the reconstruction algorithm is selected, $w(t)$ can be readily derived. For example, $w(t)$ is unit for FDK type full-scan and half-scan reconstructions because as implicated by the algorithm, all projections are considered equally weighted in the reconstruction. In the case of iterative algorithms, $w(t)$ can be derived from the cumulative contribution of the pixels of each projection in all iterative updates.

^{a)} Author to whom correspondence should be addressed. Electronic mail: ruola_ning@urmc.rochester.edu

^{b)} Dr. Binghui Zhao was a visiting professor in the Cone Beam CT Imaging Lab, Department of Imaging Sciences at the University of Rochester when this study was conducted and is an employee of Department of Radiology, Shanghai 6th People's Hospital, 600 Yishan Road, Xuhui, Shanghai, China.

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