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High-Resolution Contrast-Enhanced Cone-Beam Computed Tomography as a New Resource for In Vivo Quantitation of Intimal Hyperplasia

Lara Strittmatter, Ph.D.[1], Thomas Flood M.D., Ph.D.[2], Imramsjah M.J van der Bom Ph.D.[2] , Anna Luisa Kühn M.D.,Ph.D.[2], Ajay K. Wakhloo, M.D.[2], Mathew Gounis, Ph.D.[2], Gregory Hendricks, Ph.D.[1]

[1.] Electron Microscopy Core, Department of Cell and Developmental Biology, UMass Medical School, Worcester, MA.
[2.] New England Center for Stroke Research, Department of Radiology, UMass Medical School, Worcester, MA.

Worldwide, intracranial atherosclerotic disease (ICD) is the most common cause of stroke. In an attempt to improve the clinical outcome of patients with severe, symptomatic ICD, percutaneous transluminal angioplasty and intracranial stenting have become treatment options over the last years. Follow-up imaging of patients with ICD that underwent intracranial stenting is generally done using invasive, catheter 2D subtracted angiography. Since often the vessel path is curved and the neointimal hyperplasia (NH) is eccentric, in-stent restenosis (ISR) may be under- or overestimated using 2D techniques.

Angiographic c-arm systems do not only provide 2D fluoroscopy but also enable 3D cone-beam computed tomography (CBCT). Previously reported research has shown that by using contrast-enhanced CBCT (CE-CBCT), data acquired with a small field of view enables visualization of stent and parent vasculature with great detail [1]. Here we propose and evaluate using 3D contrast-enhanced CBCT to determine the degree of ISR in a porcine model with intracranial self-expanding stents, that are made of nickel-titanium alloys and have struts measuring approximately 80µm. The degree of ISR in the animal that underwent stenting was measured at 7 weeks using CE-CBCT and was compared to standard digital subtraction angiography (DSA). To assess the accuracy of this novel approach, CE-CBCT measurements were compared to the gold standard data obtained through histological examination of sections of the stented artery.

Experiments were approved by our IACUC. Three Wingspan stents (Stryker Neurovascular, Fremont CA) and 1 Neuroform stent (Stryker Neurovascular) were placed in both subscapular branches of the subclavian and the common carotid artery of a porcine animal model that was placed on aspirin 3 days prior to and until 6 weeks after the procedure. Before stent placement, a 2.25 or 4.5 mm (depending on caliber of artery) cutting balloon was introduced to the arterial segment of interest, inflated for approximately 2 minutes, and dragged 5 mm in proximal direction while keeping the balloon inflated to generate damage to the internal elastic lamina. Thereafter, the stent was positioned to cover the damaged portion of the artery. The animal was recovered and returned to the angiographic suite after 7 weeks for follow-up imaging. DSA and CE-CBCT data was acquired using a monoplane angiographic c-arm system (FD20, Philips Healthcare, Best, the Netherlands). CE-CBCT data was obtained with a detector size of 22 cm and using a non-binned imaging mode. During the acquisition, 15% iodinated contrast (Isovue 350; Bracco Diagnostics, Princeton, NJ) was injected with 2.5 ml/s for 23 seconds into the artery with a 3 second imaging delay. After imaging, 10 ml of heparin was administered intra-venous and the animal was sacrificed shortly thereafter. Stented vessels were explanted after perfusion/fixation using a cardiac approach under physiological pressures and were embedded in epoxy resin and sectioned for histology. Sections were cut with a Buehler Diamond saw (15 HC blade) and polished to remove saw marks and then stained with 1% Toluidine Blue and images were recorded using an Olympus AX90 w/ automated stage, and a Q-Color5 5MP digital camera system [2].

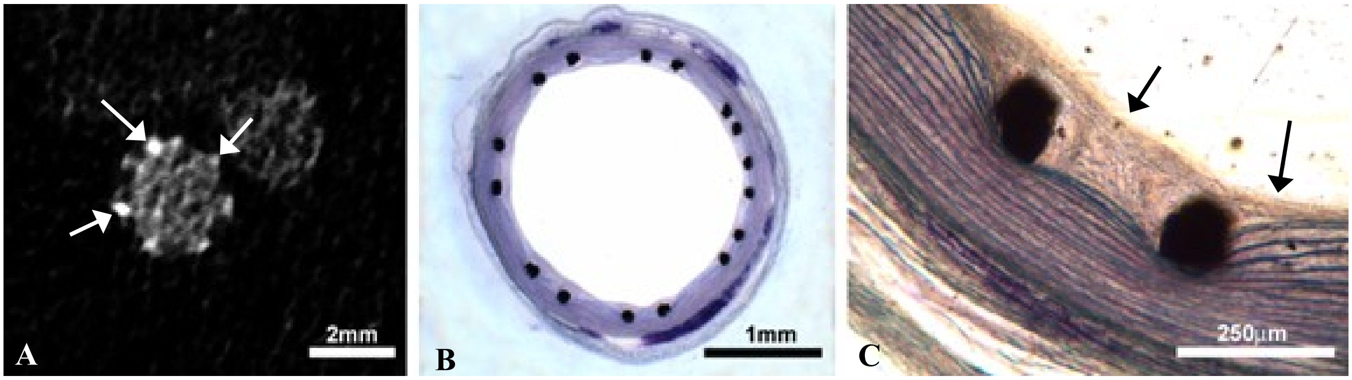

Figure 1 A-C: Stent (arrows) implanted in the porcine proximal subscapular artery. **A**, no luminal narrowing on CE-CBCT. **B**, minimal tissue growth over the stent on histological section. **C**, detail of struts with minimal NH (arrows).

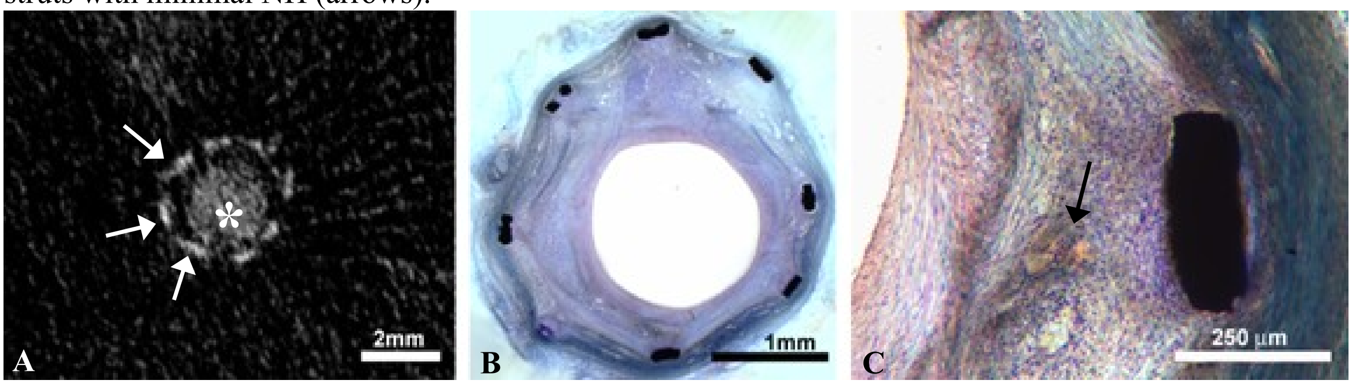

Figure 2 A-C: Stent (arrows) implanted in the porcine distal subscapular artery. **A**, apparent narrowing of the lumen (asterisk) on CE-CBCT. **B**, the apparent narrowing of the lumen in the histological section is explained by migration of the stent through a dissection into the adventitia of the arterial wall. **C**, detail of strut within the smooth muscle and adventitia layers, red blood cells (RBCs) from hemorrhage within the dissection can also be seen (arrow).

In the proximal subscapular artery, there was minimal NH detected on CE-CBCT and DSA, in correspondence with histological data (Fig. 1A-C). In contrast, a region of lumen narrowing in a branch of the distal subscapular artery could be seen with CE-CBCT (Fig. 2A). This region did not correspond to neointimal hyperplasia when sections of this vessel were analyzed (Fig.2B). The narrowing of the lumen was caused by arterial dissection during balloon injury with gradual stent migration into the dissection; which is confirmed by noted disruption of the internal elastic lamina and hemorrhage within the media of the artery (Fig.2C).

Though it is clear that CE-CBCT allows for a better recognition of luminal narrowing than does 2D fluoroscopy, it doesn't offer any information on the etiology of the event or its histopathology. However as a tool for tracking long term changes in atherosclerotic vascular disease this new imaging modality is a promising less invasive new diagnostic tool for the interventional neuroradiologist.

References

[1] NV Patel, *et al*, American Journal of Neuroradiology **32** (2011), 137-144
[2] J. Li, *et al*, Journal of Vascular Surgery **39** (2003), 1074-1083.

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