Simultaneous Non-contrast Angiography and intraPlaque hemorrhage (SNAP) imaging for atherosclerotic disease evaluation Jinnan Wang¹, Peter Börnert², Huilin Zhao³, Xihai Zhao⁴, Niranjan Balu⁵, Marina S Ferguson⁵, Thomas S Hatsukami⁵, Jianrong Xu³, Chun Yuan⁵, and William S Kerwin⁵

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Luminal stenosis remains the current clinical standard for evaluating stroke risk due to carotid disease ¹. Nevertheless, Intraplaque Introduction hemorrhage (IPH) identified in the atherosclerotic plaque has been strongly associated with increased risk of clinical events ² and plaque progression Current clinical MRA approaches, however, are unable to visualize intraplaque hemorrhage. Additionally, contrast-enhanced MRA techniques lead to the risk of NSF. To address these limitations, we propose a Simultaneous Non-contrast Angiography and intraPlaque hemorrhage (SNAP) imaging technique that allows both MRA and IPH evaluation in the same acquisition.

Methods Pulse Sequence The SNAP sequence takes advantage of the Phase-Sensitive Inversion Recovery (PSIR) sequence 4; such that the final image will present both positive and negative signals corresponding to the magnetization polarity after the inversion pulse. As shown in Fig.1, two gradient echo trains were used – one with flip angle (FA) α for data acquisition after an inversion recovery (IR) pulse, and one with 5° FA for phase sensitive reconstruction, TI is the time when the center line of the k-space is acquired, IRTR is the duration between two neighboring IR pulses.

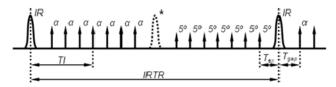


Fig. 1 The SNAP pulse sequence.

Sequence Optimization FA and TI were jointly optimized to achieve optimal IPH and lumen characterization. In a custom-programmed Bloch-equation based computer simulation, FA ranges between 5°-25° and TI ranges between 200-1000ms were tested to achieve the highest normalized magnetization (M_z/M_0) contrast between IPH_wall and wall_lumen. MR scan and post processing 13 patients (Male: 9, Female: 4) with diagnosed carotid atherosclerotic plaque were recruited after obtaining IRB approvals and informed consent. One subject also underwent endarterectomy after the MR imaging; corresponding Mallory's trichrome were obtained for IPH detection on histology. All images were acquired on a 3T clinical scanner (Philips Achieva, R3.21, the Netherlands) with a phased-array carotid coil. SNAP images were acquired in the coronal plane to cover the carotid artery with a FH coverage of 160mm. Imaging parameters were: 3D TFE, TR/TE10/4.8ms, FA/TI optimized above, resolution: 0.8×0.8×0.8mm³, interpolated to: 0.4×0.4×0.4mm³, NSA 2, imaging time: 5min17sec. The final SNAP image can be displayed as: original (Fig.2a), negative-only (Fig.2b), positive-only (Fig.2c) or a jointly-displayed color-coded version (Fig.2d). In the color-coded images, the red region corresponds to IPH. When negative signals were displayed in Fig.2b&d, the absolute values of negative values were used to determine the signal intensity. MIP images were also generated (Fig.2e) to help identify lesions and facilitate image review. Stenosis and IPH detection validation SNAP images were compared with established TOF and MP-RAGE images to validate the luminal area measurement and IPH detection accuracy. Positive-only SNAP images were used for IPH detection and negative-only SNAP images were used for lumen measurements. Images were separately reviewed with the reviewer blinded to the type of images. Pearson's correlation and Cohen's kappa were used to evaluate lumen area measurement and IPH detection, respectively.

MR scan Maximized IPH wall and wall lumen contrast were achieved when FA and TI were chosen to be 11° and 500ms. When used, the lumen presents the strongest negative signal and IPH presents the strongest positive signal. Excellent luminal and IPH delineation were obtained on all subjects (Fig.2). For the subject who underwent endarterectomy (Fig.3), remarkable agreement on both lumen and IPH delineation were found - even high risk features such as ulcers (Arrows) and high-level stenosis (Arrowheads) were accurately delineated on SNAP images. <u>Validation</u> On a slice based lumen area comparison between SNAP and TOF, very strong correlation (R=0.96) was found between the two measurements. SNAP area is slightly larger than the TOF area (SNAP: 33.29±19.37mm² vs. TOF 31.81±17.65mm², p<0.01), which is likely caused by the improved lumen delineation of SNAP. For IPH comparison, both SNAP and MP-RAGE identified the same 8 arteries as containing IPH; on a slice basis, very good agreement was also found (Cohen's kappa of 0.82, p<0.01) between SNAP and MP-RAGE measurements, although SNAP identified a few additional cases than MPRAGE (SNAP: 68, MPRAGE: 60, both: 57) which is likely due to improved sensitivity.

Conclusion The SNAP imaging technique was proposed and validated to image both luminal stenosis and intraplaque hemorrhage in atherosclerosis patients in one scan. SNAP provides more robust lumen delineation compared to regular in-flow based MRA due to its less reliance on the inflow effect; it also provides more sensitivity to IPH detection due to the expanded overall dynamic range brought by phase-sensitive reconstruction. SNAP has the potential to become the first-line imaging method in a clinical environment for stroke patient care.

Reference 1. Moore WS et al. Stroke 1995. 2. Singh N et al. Radiology 2009. 3. Takaya N et al. Circulation 2005. 4. Kellman P et al. MRM 2002.

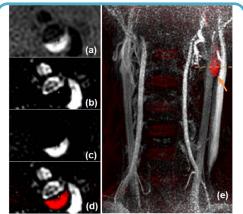


Fig. 2 Sample SNAP images and different viewing options: original (a), negative-only(b), positive-only (c), color-coded joint view (d) and the MIP of jointview (e). The arrow indicates the IPH and the line shows where images (a-d) are from.

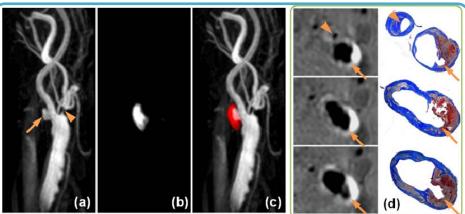


Fig. 3 3D MIP images of the MRA-portion (a), IPH-portion (b) and color-coded joint view (c) of the SNAP images. Both IPH and luminal MRA were nicely delineated throughout the 160mm coverage of bilateral carotid arteries. Even small branches of the carotid artery, high-risk features like ulceration (Arrows) and high-level stenosis (Arrowheads) were visualized. Both IPH and luminal shapes were confirmed by the matched Mallory's trichrome histology slides (d)