# **Test-Retest Reliability of Continuous Arterial Spin Labeling of Normal Parotid Glands**

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Abstract: Purpose : To compare the test-retest reproducibility of three scans for continuous arterial spin labeling (CASL). Materials and methods: In this prospective study, eight healthy subjects were scanned on 3.0 T scanner with CASL. Three scans were performed at two intervals, i.e 20 minutes and 1 week, reproducibility of continuous arterial spin at different intervals were observed, by two different readers.

Results: The average value for blood flow measurements of the parotid gland for tow readers were (Omin 52.09895, 20min 54.78945, Iweek 55.13335), Intra-observer and inter-observer data were assessed by calculating the percent coefficient of variation (% CVs) of BF(Blood Flow) after the same or other radiologists repeatedly placed ROIs(Region of Interest) on the gland areas.

Conclusion: The precision of CASL technique in measuring the blood flow of parotid gland makes it an interesting and considerable method of choice for clinical application of ASL in the future.

Key words: continuous arterial spin labeling (CASL), Parotid glands, Test-retest reproducibility. \_\_\_\_\_

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#### Introduction I.

Arterial spin labeling (ASL) perfusion MRI was invented almost 15 years ago <sup>(1-2)</sup>, but until now it has not been applied clinically on a large scale and its not applied widely in participation (3-4). ASL has several advantages over the traditional contrast techniques. Firstly, ASL dose not require contrast agent, which is particularly beneficial in patients with chronic renal failure on whom using the contrast may lead to severe complications, Hence, causes distress to the radiologist <sup>(5)</sup>, also in pediatric patients using ASL avoids needle pricks which are otherwise necessary for gaining an intravenous access to inject the contrast. Secondly, ASL is quantitative <sup>(6)</sup>whereas the available perfusion techniques are qualitative <sup>(7)</sup>. The global as well as regional assessments of cerebral perfusion are possible by quantification, also perfusion values have also shown to be corelated with histological grade of neoplasms <sup>(8,9)</sup>, the necessary post-processing has been automated with the development in scanner technology and computer processing capabilities <sup>(10,11)</sup>.

An inversion pulse is employed to tag incoming spins at a level proximal to the imaging slab, and following a transit delay to permit these labelled spins to enter the imaging plane and exchange with tissue, management and label images are obtained. once the acquisition of roughly 60 control-label volumes for signal intensity averaging, the pair-wise subtraction of those 2 images yields maps of parotid perfusion, expressed in units of mL/100 g/min. At our establishment, a completely automated post processing cascade is about off on extraction of the raw ASL data and includes knowledge transfer to network-attached storage, conversion from DICOM to Neuroimaging informatics Technology Initiative format, motion correction, tissue segmentation, flow quantification, creation of color Joint Photographic expert group (JPEG) BF (Blood Flow) maps, conversion back to DICOM format, and insertion into the clinical PACS.<sup>(12)</sup>

These steps are performed with use of distributed grid process with the Sun Grid Engine (Sun Microsystems, santaclara, Calif). Our pipeline includes automatic error-recovery with data-provenance (output logs are analyzed to initiate applicable automatic error-recovery procedures), and e-mail notifications of results and outline logs with links to JPEG images compliant with the Health information portability and accountability Act. With use of our automatic pipeline, the ultimate post processed images seem to be within the PACS inside 10 minutes once acquisition and transfer, frequently before the remainder of the conventional clinical study is completed.

This experiment has been performed in order to compare the test-retest reproducibility of three scans of continuous arterial spin labeling (CASL). The area of focus is the parotid glands of healthy individuals. The interval between the first and the second scan being 20 minutes and that between the second and the third scan being 1 week.

# II. Materials and Methods

### 1. Subjects:

Eight healthy subjects between the age group of 25-35 years volunteered for this experiment. A detailed history of the subjects were taken to exclude any past history of medical conditions. The subjects were informed about the procedure for the scan and details about the ASL. With their consent, the procedure was performed.

# 2. Imaging methodologies :

# 2.1 Data acquisition-

Imaging data were collected by using 3 Tesla scanner (GE Discovery MR, 750w,3T, Connecticut,USA) at Jiangsu province Hospital, The First affiliated Hospital Nanjing Medical University, continuous arterial spin labeling (CASL) protocols were optimized for performance and quality while maintaining similar parameters (Bilateral Parotid Gland covering with 24 axial slices, 3D EPI acquisition, labeling duration = 1516 ms, post-labeling delay = 1500 ms, sequence duration = 6 min followed by 30 minutes of interval then 5 minutes, TR/TE = 4460/17 msec, FOV =  $240 \times 240$  mm, NEX-3). T2-weighted Structural 3D axial images were acquired in the same session. The ASL sequence was acquired at rest with eyes open/closed <sup>(13)</sup>. The staff was trained to minimize subjects head and body movement.

# 2.2 Arterial spin labeling pre processing-

Perfusion data were pre processed and analyzed with the Statistical Parametric Mapping software, and a built-in script to calculate BF<sup>(14)</sup>. Functional images of each subject were at first realigned to correct for the head movement. Then, the mean image, anatomical image were co-registered and segmented. Pairwise subtraction of the label and control functional images resulted in the generation of perfusion weighted image series, then converted to absolute BF image series based on a single compartment ASL perfusion model <sup>(14,15,16)</sup>. Many factors contribute to poor quality of data of the BF image measured with ASL <sup>(17,18)</sup> for the assessment of data quality, we have used two quantitative measures generated by an automated calculation system to reduce subjective assessment .

#### 2.3 Regions of interest -

The parotid glands are the regions to be focused on for measuring the blood flowBF ratio.

#### Statistical analysis

All statistical analyses were performed using the Statistical Program for Social Sciences (SPSS) statistical software (version 18, Chicago, IL, USA). Data were expressed as mean±standard deviation, an intra class correlation coefficient (ICC) in single measure, two-way mixed model was used to examine the reliability between the 2 readers (Y.C.H and Y.H.T.) in evaluating the ASL BF maps.

# III. RESULTS

In all cases, blood flow measurements of the parotid gland were feasible using the FAIR True FISP approach. The parotid gland exhibited intermediate signal intensity (between fat and musculature) on T2-weighted Structural 3D axial images in all volunteers. Precise delineation of the parotid gland for ROI positioning was possible in all cases. The appearance of the parotid gland in the subtracted FAIR True FISP images and in the derived blood flow maps were rather homogeneous, but this homogeneous background signal was superimposed by some local spots with higher blood flow rates due to larger supplying vessels.

No statistically significant difference between the right and left parotid were observed in baseline and peak tissue blood flow data.

# Intra-Subject Variability of BF Values:

BF values often Nosignificantly differed between the left and right glands in the same individuals and SBF types of the left and right glands were different in some individuals. Therefore, we assessed the intrasubject variability by calculating percent differences in BF values between the left and right glands and then compared the percent differences in BF values between different subject groups with different readers and different scans of left and right parotid glands in the same individuals. We found no significance different in BF values in different readers or different scan time, as shown in Table(1).

Ν	AVG	STDEV
16	51.3125	17.21421
16	53.0000	16.36867
16	53.2813	20.29612
	N 16 16 16	N AVG   16 51.3125   16 53.0000   16 53.2813

Reader2 1week	16	56.9854	19.94844		
Reader2 20min	16	56.5789	15.36924		
Reader2 0min	16	52.8854	15.85715		

Table 1.BF value

# Intra-observer, Inter-observer and Test-retest repeatability of BF Values:

Intra-observer and inter-observer data were assessed by calculating the percent coefficient of variation (% CVs) of BF after the same or other radiologists repeatedly placed ROIs on the gland areas. For the intraobserver error assessment, one radiologist placed an ROI onto each of the gland areas of SBF maps that were obtained from 10 left parotid glands (10 control subjects); for the inter-observer error assessment, two radiologists including the one who participated in the intra-observer assessment repeatedly (3 times) placed ROIs onto each of the gland areas of the same BF maps (n = 10). The average % CVs were calculated from the BF data obtained from different glands (intra-observer errors) and different observers (inter-observer errors). Table (2).

BF:

ICC	Inter-observe	Intra-observer
0min	0.978 ( 0.940~0.992 )	0.997 ( 0.992~0.999 )
20min	0.978 ( 0.937~0.992 )	0.996 ( 0.989~0.996 )
1 week	0.976 ( 0.932~0.991 )	0.999 ( 0.997~1 )
<b>Table 2. Intra-observerICC</b> : Reader1; 1 <sup>ST</sup> read Vs. 2 <sup>nd</sup> read; 3 scans (0 min, 20 min, 1 week)		

Inter-observer ICC: (Reader 1, the average of 1st and 2nd read) Vs. (Reader 2); 3 scans (0 min, 20 min, 1 week)

The majority of parotid glands regions has excellent BF reliability in different scans at different times as shown in Table (3).

ICC	Test-retest repeatability
0-20 min	0.935 (0.813 ~0.977)
0min-1week	0.927 (0.792 ~0.975)
20min-1 week	0.944 (0.841~0.981)

**Table 3. Test-retest repeatability ICC**: Reader 1; the average of 1st and 2ndreading; 1<sup>st</sup> scan VS 2<sup>nd</sup> scan; 1<sup>st</sup> scan VS 3<sup>rd</sup> scan; 2<sup>nd</sup> scan VS 3<sup>rd</sup> scan

# IV. Discussion

In ASL, the water in arterial blood is magnetically labeled then the image is taken. At first, the arterial blood water is magnetically labeled just below the slice of interest by applying an inversion pulse of 180 degree radiofrequency. This results in the inversion of the total magnetization of the blood water. To understand in a better way, the water molecules in the arterial blood are magnetically labeled, after particular period of time called the transit time, the paramagnetic tracer flows into the region or slice of interest where the exchange occurs with the tissue water. The inflow of inverted spins into the blood water alters the net tissue magnetization, thereby, reduces it as well as the MR signal and image intensity. At this time, an image is taken and is called the tag image. Another image called the control image is created by repeating the experiment without labeling the arterial blood water. A perfusion image is produced by subtracting the control image and the tag image [1]. In this image, the amount of arterial blood that is delivered to each area within the transit time is reflected <sup>(19)</sup>.

Presently, there are four types of ASL techniques : pulse ASL (PASL), continuous ASL (CASL), pseudo-continuous ASL (PCASL), and velocity-selective ASL (VS-ASL). The main difference between these categories is the technique which magnetically tags the inflowing blood. These have been developed in order to address the technical challenges and limitations in the implementation of ASL earlier.

Our study assessed the influence of three different scans and different readers on the measurement of MRI derived parameters.

The mean  $\pm$  SD BF values obtained with all three scans were excellent agreement with prior ASL study. as well as BF values measured from CASL were significantly good in the three scans, the labeling plane of CASL typically lies in the inhomogeneous region of the Tx/Rx head coil, it is possible that inversion efficiency may vary considerably between subjects.

For reproducibility assessment the current utilize of ICC is for two reasons, firstly it is commonly reported in other studies, which makes it easier to compare results, secondly it provides an unbiased measurement of reproducibility since it is normalized to the mean of the measurements. As is evident from the

table 1 and 2, reproducibility declined with increasing rescan intervals, this result is not surprising, given how the three rescan interval are sensitive to virous contributions of error to the ASL experiment, the within session reproducibility, primarily sensitive to scanner instabilities and errors induced by data processing, was indeed the highest.

This was followed by the 20 minutes reproducibility, which includes repositioning errors. Finally, the one-week reproducibility which includes both physiological fluctuations and repositioning errors, was the lowest.

Of the three scans CASL demonstrated excellent reproducibility for the measurements made after volunteers repositioning. The range of intra-observer and inter-observer ICC for the current study is totally within the normal range.

This finding indicates major signal contributions from microscopic vessels with a rather homogeneous spatial distribution, while larger arteries or veins became visible as hot spots in the blood flow maps. Precise delineation of the parotid gland and exclusion of large vessels for ROI positioning was possible in all cases. Disadvantages of our study were limited studies on ASL for parotid gland, Limited number of volunteers.

# V. Conclusion

Our study demonstrates the excellent reproducibility of CASL, Including the ability to use high sensitivity array coils, high SNR and tagging efficiency. This high precision makes CASL an attractive method for BF measurements in clinical settings.

The precision of CASL in measuring the cerebral blood flow makes it an interesting and considerable method of choice for clinical application of ASL in the future..

# **Conflict of interest disclosure**

We declare that we have no conflict of interest.

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