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COMPARISON OF QUIESCENT INFLOW SINGLE-SHOT AND NATIVE SPACE FOR NONENHANCED PERIPHERAL MR ANGIOGRAPHY

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Abstract

Purpose—To evaluate two nonenhanced MRA methods: quiescent-interval single-shot (QISS) and Native SPACE (NATIVE= Non-contrast Angiography of the Arteries and Veins; SPACE = Sampling Perfection with Application Optimized Contrast by using different flip angle Evolution), using contrast-enhanced MR angiography (CEMRA) as a reference standard.

Materials and Methods—20 patients (14 male, mean 69.3 years old) referred for lower extremity MRA were recruited in a HIPAA-compliant prospective study. QISS and Native SPACE of the lower extremities were performed at 1.5T with a hybrid dual-injection contrast-enhanced MRA as reference. Image quality and stenosis severity were assessed in segments by two blinded radiologists. Methods were compared with logistic regression for correlated data for diagnostic accuracy.

Results—Of 496 arterial segments, 24 were considered non-diagnostic on the Native SPACE images. There were no QISS or CEMRA imaging segments considered to be non-diagnostic. Image quality was significantly higher for QISS than for Native SPACE. QISS stenosis sensitivity (84.9%) was not significantly different from Native SPACE (87.3%). QISS had better specificity (95.6%) than Native SPACE (87.0%), $p=0.0041$. In comparison with QISS, Native SPACE proved less robust for imaging of the abdominal and pelvic segments.

Conclusion—Native SPACE and QISS were sensitive for hemodynamically significant stenosis in this pilot study. QISS NEMRA demonstrated superior specificity and image quality, and was more robust in the abdominal and pelvic regions.

INTRODUCTION

The availability of accurate noninvasive tests has decreased the need for preoperative digital subtraction angiography (DSA) in the evaluation of peripheral arterial disease (PAD) (1). The ankle brachial index is sensitive for hemodynamically significant PAD (2) and can be performed in conjunction with Doppler waveform analysis and segmental pressure measurement in an effort to increase accuracy. Accuracy is limited nonetheless in patients with calcified vessels e.g. in diabetic patients and those with renal insufficiency (3). Computed tomographic angiography (CTA) offers high spatial resolution and short scan times without the risks associated with an invasive procedure (4). The reported sensitivity of CTA for greater than 50% stenosis is on the order of 89%-100% with specificity reported at

92%-100% (2). CTA has the disadvantage of exposing patients to ionizing radiation and there is also the associated risk of contrast-induced nephropathy (CIN), which is of particular concern given the frequency of renal dysfunction in patients with PAD (5). In a systematic review of the published literature, contrast-enhanced magnetic resonance angiography (CEMRA) was shown to be highly accurate for detection of stenosis greater than 50% within the lower extremity arterial tree (5). Physiologic testing is insufficient for preoperative revascularization planning in these patients, regardless of whether endovascular or open techniques are considered. Until the administration of gadolinium-based contrast agents was linked with nephrogenic systemic fibrosis (NSF) (6), CEMRA was often the test of choice in patients with chronic kidney disease.

Nonenhanced MRA (NEMRA) avoids the potential risks of NSF and CIN, as well as ionizing radiation. Nonenhanced 2D time of flight methods have been available for decades (7). However, lengthy acquisition times (typically approaching an hour or more) and image artifacts have to date limited their routine use in favor of contrast enhanced techniques. Newer subtractive approaches for NEMRA of the peripheral arteries have been proposed which allow efficient depiction of arteries over large fields of view and suppress venous signal. These include ECG-gated 3D fast spin-echo imaging (such as fresh blood imaging [FBI] (8) and Native SPACE [NATIVE= Non-contrast Angiography of the Arteries and Veins; SPACE = Sampling Perfection with Application Optimized Contrast by using different flip angle Evolution] (9)), as well as variants predicated on 3D balanced steady-state free precession (10). Of these, fast spin echo techniques have undergone the most clinical validation and are commercially available.

Recently, an alternative non-subtractive technique called quiescent interval single shot (QISS) was described (11). Initial reports suggest that QISS can evaluate PAD with accuracy comparable to that of CEMRA (12,13). To date, the potential benefits and drawbacks of subtractive and non-subtractive nonenhanced MRA have not been evaluated. We therefore performed a pilot study, using CEMRA as the gold standard, in which the two NEMRA techniques, QISS and Native SPACE, were directly compared.

MATERIALS AND METHODS

This prospective study was institutional review board (IRB) and HIPAA compliant and informed consent was obtained from all patients. Between August 2010 and January 2012, 20 patients referred for evaluation of chronic lower limb ischemia underwent three studies within the same scan session: QISS, Native SPACE, and CEMRA (Table 1). The order in which QISS and Native SPACE was performed was randomized, with CEMRA performed afterwards. Patients who had symptoms attributable to chronic lower limb ischemia and/or abnormal ankle brachial indices met the inclusion criteria. Exclusion criteria included a history of peripheral bypass surgery, an estimated glomerular filtration rate (eGFR) < 30 ml/min/1.73 m², and standard contraindications to MRI. Stented segments were excluded from analysis.

Imaging Protocol

Imaging was performed on a 1.5 T scanner (MAGNETOM Avanto, Siemens Healthcare, Erlangen, Germany). A 16 channel peripheral vascular coil, a 6 channel body array coil, and a 4 channel flex coil were placed anterior to the subject, while a 24 channel spine array coil was placed posterior to the subject.

For all 20 subjects, the lower extremity peripheral arteries were imaged from the level of the lower pelvis to the calves (24 segments). Due to time constraints for acquiring data with all three techniques, the abdominal/pelvic region (from approximately the level of the renal

arteries to the level of the femoral heads) was only imaged in a subgroup of 5 subjects (additional 5 segments).

Native SPACE Technique—Native SPACE used the following imaging parameters: ECG-gated 3D single shot fast spin echo pulse sequence with spatial resolution (before interpolation) of $1.6\text{ mm} \times 1.6\text{ mm} \times 1.7\text{ mm}$ and a 320×320 matrix in the thigh and spatial resolution of $1.2\text{ mm} \times 1.3\text{ mm} \times 1.4\text{ mm}$ using a 384×384 matrix in the calf, coronal acquisition plane, field of view $500\text{ mm} \times 393\text{ mm}$, GRAPPA (GeneRalized Autocalibrating Partially Parallel Acquisition) parallel acceleration factor of 2, 6/8 partial Fourier, TE=20 ms, bandwidth: 977 Hz/Px, 2 echo trains per partition, (8). In all subjects, Native SPACE was acquired through the thigh and calf, with 50 mm of overlap between the two table positions. Based on empirical studies in healthy volunteers and patients, the flip angle for the thigh station was 120 degrees and for the lower station was 90 degrees. In the subgroup in whom an additional abdominal/pelvic station was acquired, imaging parameters were as follows: spatial resolution of $1.6\text{ mm} \times 1.6\text{ mm} \times 1.7\text{ mm}$ and a 320×320 matrix, coronal acquisition plane, FOV $500\text{ mm} \times 393\text{ mm}$, GRAPPA parallel acceleration factor of 2, 6/8 partial Fourier, TE = 20ms, BW: 977Hz/Px, 2 echo trains per partition, and a flip angle of 120 degrees. Data were acquired during quiet breathing.

The time delay after the R-wave for peak arterial flow for each Native SPACE acquisition was determined using a cine 2D phase contrast acquired at the level of the infra-renal aorta, tibial plateau, and 5 cm below the femoral heads, respectively. The 2D phase contrast acquisition used a velocity-encoding sensitivity of 80 cm/s for the calf region, 100 cm/s for the thigh region, and 150 cm/s for the aorta with TR = 31 ms and flip angle = 30 degrees. If the time delay for peak arterial flow differed between the two legs, the longer delay was used. Inline subtraction of diastolic phase bright blood images (using trigger delay of 0) and systolic phase dark blood images (using a trigger delay aligned with peak arterial flow) was used. For a nominal heart rate of 72 beats/min, total scan time was approximately 7-8 minutes for the calf and thigh stations with shimming accounting for up to 1.5 minutes of this time. Additional scan time for the abdomen/pelvis was approximately 2 minutes.

QISS Technique—QISS used the following imaging parameters: ECG-gated 2D single shot balanced steady-state free precession, one slice per heartbeat, $1.0\text{ mm} \times 1.0\text{ mm}$ in-plane resolution, 48 3-mm thick slices per station, no overlap, six stations per patient, field of view of $400\text{ mm} \times 320\text{ mm}$, GRAPPA parallel acceleration factor of 2, 5/8 partial Fourier with center-to-out k-space ordering, TE=1.4 ms, bandwidth: 658 Hz/Px, flip angle=90°, and fat suppression (11). For the abdominal and pelvic stations, a breath-hold of approximately 10-15 seconds was used for each group of slices, depending on heart rate. Two additional high resolution QISS stations consisting of 128 1.2-mm thick slices with 20% overlap were used to cover the popliteal trifurcation and upper calf. For a nominal heart rate of 72 beats/min, total scan time was approximately 11 minutes, with shimming accounting for up to 4 minutes of this time. The average scan time for the abdomen/pelvis station was approximately 2 minutes and for the thigh/calf station was approximately 5 minutes.

CEMRA Technique—The CEMRA protocol consisted of a time-resolved CEMRA through the calf and stepping table MRA for the remainder of the peripheral vascular system. The contrast agent was gadopentetate dimeglumine (Magnevist, Bayer, Berlin, Germany), administered intravenously followed by a saline chaser. A time-resolved coronal fast low angle shot-based sequence (TWIST – time-resolved angiography with interleaved stochastic trajectories) (14) was obtained through the calf using an injection rate of 2 mL/sec for 5-8 mL of contrast agent, parallel acceleration factor of 2, TR/TE = 3 ms/1 ms, spatial resolution of 1.9 mm (slice thickness) $\times 1.1\text{ mm} \times 1.3\text{ mm}$. A total of 15 phases were run, being one whole matrix (mask) scan and 14 post-injection ones. The acquisition time for the

mask was 18 s and for the additional phases was 5.8 s per phase. The total scanning time was 1.7 min. For the stepping table acquisition, a 1- to 2-mL test bolus was used to determine timing. Three stations were acquired before and after contrast administration using TR/TE/flip angle = 3 ms/1 ms/20°, 50-cm field of view, slice thickness of 1.5mm, in-plane spatial resolution of 1mm × 1mm, parallel acceleration factor of 2, 22 sec per station. A dual-phase infusion protocol administered 0.14 mmol/kg of the contrast agent, initially at 1.5 mL/sec, followed by 0.6 mL/sec. The subtracted images were processed using a maximum intensity projection for interpretation. Breath holding was used for the abdominal and pelvic station.

Image Analysis

Two radiologists (E.V.W and A.R.P) with at least four years of experience reading MRA independently evaluated the QISS, Native SPACE, and CEMRA studies and were blinded to each other assessment. The study order was randomized for the readings. The readers evaluated the NEMRA images independently; a consensus approach was used for the CEMRA. For comparison purposes, each study was divided into 24 anatomic segments, which included the following segments for each side: common femoral artery, profunda femoris artery, proximal and distal superficial femoral artery, popliteal artery, tibioperoneal trunk, proximal and distal anterior tibial artery, proximal and distal posterior tibial artery, proximal and distal peroneal artery; an additional 5 segments were analyzed in the subgroup where the abdomen and pelvis were included; the infra-renal abdominal aorta, common iliac artery, external iliac artery. Radiologists independently evaluated 2D source partitions, maximum intensity projections and volume-rendered 3D images for the presence of disease in each of the segments with no other clinical information provided with the images. The American College of Radiology grading system from a prior multi-institutional trial of peripheral MRA was used (15): 0, normal; 1, minimal stenosis of less than 50%; 2, one lesion with 50% or greater stenosis; 3, more than one lesion with 50% or greater stenosis; and 4, occlusion. Failure to visualize a segment which was present in the CEMRA was considered an incorrect assessment for the NEMRA technique. The feet were not included in the analysis since they were not typically within the field of view of the time-resolved CEMRA or of the peripheral array coil.

The diagnostic quality of images was graded on a scale of 0-4: 0, non-diagnostic; 1, poor quality and observer not confident; 2, fair quality and observer marginally confident; 3, good quality and observer confident; and 4, excellent quality and observer highly confident. P values of less than .05 were considered to indicate a significant difference. Using the combination of TWIST and stepping table CEMRA as the reference standard, the sensitivity, specificity, accuracy, and positive and negative predictive values for Native SPACE and QISS were evaluated for the detection of significant (≥ 50%) stenosis. 95% confidence intervals (CIs) were calculated for sensitivity and specificity.

Statistical Analysis

All statistical analyses were performed by using commercially available software (SPSS, version 18.0; SPSS, Chicago, IL). The performance of NEMRA with CEMRA as reference was analyzed for the infra-inguinal regions in all 20 subjects on a per segment, per region, and per limb basis. For the per region analysis, the segments were grouped in the following regions for each patient: aorta, pelvis, thigh, and calf. A generalized estimating equations (GEE) model was used for the segmental and regional analyses, since the probability of having PAD in one segment was not independent from the presence of disease in other segments. An unstructured binomial logit GEE model was used. For the per-region analysis the segment grades were averaged for each region (calf, thigh, abdomen/pelvis). For

CEMRA, the highest grade—indicating the more severe stenosis—was considered the diagnostic grade and was used in the analysis.

The sensitivity and specificity of QISS versus CEMRA and Native SPACE versus CEMRA were based on a binomial separation defined as non-significant stenosis less than 50% and significant stenosis greater than or equal to 50%. Raw sensitivity and specificity for each reviewer were calculated per segment. The measures of sensitivity and specificity reflected the performance of NEMRA versus CEMRA separately, while the resulting mean summary measure, standard deviation, and confidence intervals (CIs) fully accounted for the correlations between adjacent stenoses per leg. The sensitivity for NEMRA versus CEMRA was defined as the probability of detecting a stenosis given that the patient has a stenosis at each arterial level, with the assumption that NEMRA and CEMRA theoretically will perform equally at each level. This did not preclude the fact that if a stenosis was found at a particular level, the likelihood of another stenosis nearby would be increased, as reflected with the GEE model. GEE was employed only for the segmental and regional analyses. Limbs were considered independent.

For each of the NEMRA techniques, the proportion of infra-inguinal segments in which the severity of stenosis grade differed by more than 1 from the CEMRA was calculated for each reader and compared with the chi-square test.

Scores of diagnostic image quality were compared by using the Wilcoxon test and were reported as means $\pm$ standard deviations. For assessment of inter-observer variability, the agreement between the readers regarding the stenosis severity determined with each MR angiography technique was evaluated by using Cohen κ values. A κ value of 0.20 or lower implied poor agreement; values of 0.21-0.40, fair agreement; values of 0.41-0.60, moderate agreement; values of 0.61-0.80, substantial agreement; and values of 0.81-1.00, almost perfect agreement. $P < 0.05$ was considered to indicate statistical significance.

For the analysis of the abdominal and pelvic vessels, the proportion of correct diagnosis was calculated for each NEMRA method by dividing the number of segments correctly diagnosed by that method by the total number of evaluated segments. The proportions of correct diagnoses were compared with the McNemar test. The image quality scores for the abdominal and pelvic regions were compared with the paired-t test.

RESULTS

Infra-Inguinal Vessels

Between August 2010 and January 2012, 20 patients (14 men, 6 women; mean age 69.3 ± 11.7 years; age range 41-91 years) met the inclusion criteria for study participation (Table 1). A total of 40 limbs, 65 regions, and 495 infra-inguinal segments were evaluated for stenosis degree and diagnostic image quality. Five segments had prostheses and one had a stent; these were dropped from the analysis. Classification of segments by individual reader is given in Table 2. Twenty-four segments were considered non-diagnostic by NATIVE. There were no QISS or CEMRA imaging segments considered non-diagnostic. Diagnostic performance of NEMRA in the detection of lower extremity arterial stenosis is summarized in Table 3. Clinical examples are shown in Figures 1-3.

Diagnostic Performance of NEMRA Versus CEMRA

On a segmental basis, the sensitivities were not significantly different, whereas QISS showed significantly better specificity ($p=0.0041$). The sensitivities and specificities for the two NEMRA techniques were not significantly different in the per-limb and regional analyses.

Comparison of Scores for Diagnostic Image Quality

The mean scores were significantly higher for QISS at 3.2 ± 1.0 versus Native SPACE at 2.5 ± 1.1 ($p=0.0001$).

Inter-reader Agreement

Almost perfect agreement between the two readers regarding stenosis scores was achieved, with Cohen κ values of greater than 0.80 for all MR angiography techniques with $\kappa = 0.883$ for QISS and $\kappa = 0.855$ for Native SPACE MRA. When converting the percent stenosis into the binary outcomes ($\geq 50\%$ and $<50\%$) the agreement even improved, with $\kappa = 0.982$ for QISS and $\kappa = 0.982$ for Native SPACE.

For both readers, there was a significant difference between QISS and Native SPACE for the proportion of segments in which the severity of stenosis grade differed by more than 1 from the CEMRA. For reader 1, the QISS proportion was $5.2\% \pm 1.0\%$ versus $10.1\% \pm 1.4\%$ for Native SPACE ($p=0.006$). For reader 2, it was $4.6\% \pm 0.9\%$ versus $9.8\% \pm 1.2\%$ for QISS and Native SPACE, respectively ($p=0.001$).

Abdominal and Pelvic Vessels

Five patients had their abdominal and pelvic arteries evaluated with all techniques. A total of 25 arterial segments were evaluated for the presence of hemodynamically significant stenosis. One patient had a left hip metallic prosthesis, which caused susceptibility artifact that precluded evaluation of one segment (left external iliac artery). This segment was dropped from the analysis. From the remaining 24 segments, none had hemodynamically significant stenoses as assessed by CEMRA. QISS correctly evaluated all segments. For QISS, five segments were graded as having good image quality, and the remainder was graded as having excellent image quality. Native SPACE incorrectly classified a normal segment as having a hemodynamically significant stenosis. Four segments imaged with Native SPACE were considered non-diagnostic, corresponding to 16.7% of the imaged segments. Fifteen segments were graded as having poor image quality and five as having fair image quality. QISS had a higher proportion of correct diagnosis at 100% versus 79.2% for Native SPACE, although the difference did not reach statistical significance.

The image quality for QISS in the abdominal and pelvic stations was significantly higher at 3.8 ± 0.5 versus 1.0 ± 0.7 for Native SPACE ($p=0.0046$).

DISCUSSION

In comparison with CEMRA of the peripheral arteries, there has been substantially less clinical experience with NEMRA. Native SPACE is commercially available, whereas QISS is currently only available as a work-in-progress technique. As a 3D fast spin-echo technique, Native SPACE can acquire higher spatial resolution, is insensitive to static field inhomogeneities, and can depict branching vessels regardless of orientation relative to the head-foot direction. By comparison, QISS does not require patient-dependent modification of imaging parameters, and as a non-subtractive single-shot 2D acquisition is less sensitive to motion. It also permits breath-holding for the abdominal and pelvic regions, thereby reducing the risk of motion artifacts.

In this pilot study, both QISS and Native SPACE proved sensitive for PAD. The sensitivity of QISS is comparable to a recent report in a large patient series (12). The sensitivity of Native SPACE is also comparable to a previous report using a subtractive 3D fast spin-echo technique (16). Although the sensitivities of the two NEMRA techniques were similar, QISS showed superior specificity and positive predictive value. Image quality for QISS was also

significantly better. In some cases, Native SPACE severely exaggerated the extent of disease due to poor image quality (due to patient motion, incorrect timing with respect to peak systolic flow, or excessive diastolic flow-related dephasing). These artifacts largely accounted for the suboptimal Native SPACE image quality, which accounted for some segments being graded as non-diagnostic. This was most problematic in the proximal thigh segments. Moreover, the proportion of segments in which the severity of stenosis grade differed by more than 1 from the CEMRA was approximately twice as great for Native SPACE as for QISS.

There were a few potentially significant technical challenges in this study. One limitation is that occluded segments may appear slightly exaggerated in extent compared with CEMRA. The reason for this artifact is uncertain, but it might relate to extremely slow or absent flow within the patent portion of the vessel beyond the occlusion. It might also relate to the presence of reversed flow within the patent portion arising from collaterals. A limitation of the QISS MRA technique is a lack of sensitivity to reversed blood flow and partial volume averaging for horizontally oriented vessels. The patent portion appears occluded due to the directional saturation effect of the QISS venous saturation pulse. A second limitation is occasional mistriggering of the sequence in the abdomen due to RF interference when the ECG gating box is positioned near the magnet bore.

Due to time constraints, the abdominal and pelvic regions were only imaged in a small subgroup of subjects. However, it was evident that image quality for Native SPACE was degraded compared to the thigh and calf regions. Diastolic flow is continuous in the aorta so that it can be challenging to obtain a bright blood data set with Native SPACE. Moreover, data are acquired during breathing so that misregistration artifact may occur. By contrast, QISS is less sensitive to flow patterns, permits breath-holding, and image subtraction is not used. As an alternative to Native SPACE, non-subtractive 3D balanced SSFP techniques have been proposed. For instance, a quadruple inversion recovery 3D balanced SSFP method demonstrated excellent image quality for the abdominal and pelvic regions (17).

It is likely that better image quality could be obtained with Native SPACE by additional calibration steps tailored to specific regions and repeating scans when motion artifact was noted. However, such maneuvers were not practical within the time constraints of this study. Also, it is not necessarily appropriate to extrapolate our results to comparable NEMRA techniques provided on MR systems produced by other vendors. However, certain aspects of the technique, such as sensitivity to patient motion, are likely intrinsic to any subtractive 3D NEMRA approach.

In conclusion, NEMRA offers an alternative to contrast-enhanced CTA and MRA for the evaluation of symptomatic chronic lower limb ischemia, particularly when the administration of iodinated or gadolinium-based contrast agents is contraindicated. Our results indicate that both Native SPACE and QISS are sensitive for hemodynamically significant stenosis, and that QISS NEMRA may be advantageous due to improved specificity and image quality.

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Figure 1.

a) CEMRA with superimposed TWIST of the calf vessels, b) QISS, c) Native SPACE images in a 76 year-old female smoker with claudication and hypercholesterolemia. Segmental occlusion of the proximal right anterior tibial artery was identified on all three sequences (arrowheads) with two vessel runoff to the ankle. There was three-vessel runoff on the left. Both readers incorrectly identified a hemodynamically significant stenosis (arrow) of the right common femoral artery on the Native SPACE images. Artifact in the left calf in the Native SPACE images resulted in a poor Likert score for this region. (There was also a segmental occlusion of the left external iliac artery; however, the abdominal and pelvic regions were not fully imaged with Native SPACE in this subject so were excluded from analysis.)

Figure 2.

a) CEMRA with superimposed TWIST of the calf vessels, b) QISS, c) Native SPACE images in a 66-year-old male smoker with right sided claudication (the patient has a stent in the distal right superficial femoral artery, so that this segment was excluded from analysis [curved arrows]). Multiple 50% stenoses in the right anterior and posterior tibial arteries, and occlusion of the left posterior tibial artery were identified on CEMRA and QISS images. Both readers incorrectly identified occlusion of the proximal left anterior tibial artery on the Native SPACE images (arrow). Lack of arterial visualization in the right calf with Native SPACE resulted in a non-diagnostic Likert score, as did motion artifact in the abdominal/pelvic region.

Figure 3.

a) CEMRA with superimposed TWIST of the calf vessels, b) QISS, c) Native SPACE images in a 54-year-old female smoker with claudication, diabetes, and hypercholesterolemia. Both readers identified segmental occlusions in the right and left superficial femoral arteries (arrows) and occlusion of the left anterior tibial artery (arrowheads) with all techniques. There is motion artifact in the left calf and right pelvis in the Native SPACE images, resulting in poor Likert scores.

Table 1

Subject characteristics

Demographics	
Mean age (years)	69.3
Smoking %	85% (17/20)
% Female	30% (6/20)
Symptomatic	80% (16/20)
Diabetes	30% (6/20)
Dyslipidemia	65% (13/20)

Table 2

Classification of segments by each reader

	Less than 50% stenosis	50% or greater stenosis	Non-diagnostic
QISS Reader 1	379	111	0
QISS Reader 2	372	118	0
Native Reader 1	333	138	24
Native Reader 2	331	135	24
CEMRA Reader 1	368	122	0
CEMRA Reader 2	368	122	0

Table 3

Generalized estimation equation modeling (combined reader grades) of nonenhanced MR angiography versus contrast enhanced MR angiography for segments and regions.

	Combined Reader Segmental				Combined Reader Regional			
	QISS		NATIVE		QISS		NATIVE	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Sensitivity	84.9%	11.7%	87.3%	21.7%	90.8%	4.5%	88.3%	4.6%
Specificity	95.6%	4.5%	87.0%	7.4%	94.5%	10.8%	82.0%	14.4%
PPV	88.5%	10.3%	65.3%	30.6%	90.8%	12.9%	76.1%	41.8%
NPV	95.7%	4.9%	93.9%	4.3%	94.5%	6.6%	92.5%	10.9%