AD_____

MIPR NUMBER 95MM5554

TITLE: Magnetic Resonance Mammography (MRM): A Promising Application for Fat Suppression by Phase Unwrapping in the 3-Point-Dixon Method

PRINCIPAL INVESTIGATOR: MAJ Vincent B. Ho

CONTRACTING ORGANIZATION: Madigan Army Medical center
Tacoma, Washington 98431-5000

REPORT DATE: July 1996

TYPE OF REPORT: Final

PREPARED FOR: Commander
U.S. Army Medical Research and Materiel Command
Fort Detrick, Frederick, Maryland 21702-5012

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. AGENCY USE ONLY (Leave blank)	2. REPORT DATE	3. REPORT TYPE AND DATES COVERED
	July 1996	Final (5 Dec 94 - 30 Jun 96)

4. TITLE AND SUBTITLE
Magnetic Resonance Mammography (MRM): A Promising Application for Fat Suppression by Phase Unwrapping in the 3-Point-Dixon Method

5. FUNDING NUMBERS
95MM5554

6. AUTHOR(S)
MAJ Vincent B. Ho

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
Madigan Army Medical Center
Tacoma, WA 98431-5000

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)
U.S. Army Medical Research and Materiel Command
Fort Detrick, MD 21702-5012

10. SPONSORING/MONITORING AGENCY REPORT NUMBER

11. SUPPLEMENTARY NOTES

12a. DISTRIBUTION/AVAILABILITY STATEMENT
Approved for public release; distribution unlimited

12b. DISTRIBUTION CODE

13. ABSTRACT *(Maximum 200 words)*

Purpose: This study was undertaken (1) to further develop Phase Unwrapping in the 3-Point-Dixon Method (PU3PD) for Magnetic Resonance Mammography (MRM) on a v. 5.4 GE Signa 1.5 T MRI scanner, (2) to compare the PU3PD technique to conventional methods for fat signal elimination (subtraction 3D SPGR and FATSAT) in MRM. Subjects and Methods: 17 female patients (32-74 years; mean 48.76 years) with 18 mammographically suspicious lesions were enrolled. 18 sets of unilateral 3D SPGR and PU3PD images and 11 sets of bilateral FATSAT and PU3PD images were obtained following i.v. gadolinium contrast media administration. Results: PU3PD was preferred 89% over subtraction 3D SPGR and 73% over FATSAT images for fat elimination and 89% and 55% for lesion characterization. Pathologic confirmation was available for 15/18 lesions. PU3PD afforded improved lesion characterization than 3D SPGR as PU3PD images were not plagued by subtraction artifact. Bilateral FATSAT and PU3PD, performed at the end of each study both afforded suboptimal lesion/region characterization. Conclusion: PU3PD can provide better fat signal elimination than subtraction 3D SPGR and FATSAT. Lesion morphology on PU3PD images can be superior to subtraction 3D SPGR. PU3PD was developed for a v. 5.4 GE Signa 1.5 T MRI scanner.

14. SUBJECT TERMS	15. NUMBER OF PAGES
Defense Women's Health Research Program	15
	16. PRICE CODE

17. SECURITY CLASSIFICATION OF REPORT	18. SECURITY CLASSIFICATION OF THIS PAGE	19. SECURITY CLASSIFICATION OF ABSTRACT	20. LIMITATION OF ABSTRACT
Unclassified	Unclassified	Unclassified	Unlimited

GENERAL INSTRUCTIONS FOR COMPLETING SF 298

The Report Documentation Page (RDP) is used in announcing and cataloging reports. It is important that this information be consistent with the rest of the report, particularly the cover and title page. Instructions for filling in each block of the form follow. It is important to ***stay within the lines*** to meet ***optical scanning requirements***.

Block 1. Agency Use Only *(Leave blank)*.

Block 2. Report Date. Full publication date including day, month, and year, if available (e.g. 1 Jan 88). Must cite at least the year.

Block 3. Type of Report and Dates Covered. State whether report is interim, final, etc. If applicable, enter inclusive report dates (e.g. 10 Jun 87 - 30 Jun 88).

Block 4. Title and Subtitle. A title is taken from the part of the report that provides the most meaningful and complete information. When a report is prepared in more than one volume, repeat the primary title, add volume number, and include subtitle for the specific volume. On classified documents enter the title classification in parentheses.

Block 5. Funding Numbers. To include contract and grant numbers; may include program element number(s), project number(s), task number(s), and work unit number(s). Use the following labels:

C	- Contract	**PR**	- Project
G	- Grant	**TA**	- Task
PE	- Program Element	**WU**	- Work Unit Accession No.

Block 6. Author(s). Name(s) of person(s) responsible for writing the report, performing the research, or credited with the content of the report. If editor or compiler, this should follow the name(s).

Block 7. Performing Organization Name(s) and Address(es). Self-explanatory.

Block 8. Performing Organization Report Number. Enter the unique alphanumeric report number(s) assigned by the organization performing the report.

Block 9. Sponsoring/Monitoring Agency Name(s) and Address(es). Self-explanatory.

Block 10. Sponsoring/Monitoring Agency Report Number. *(If known)*

Block 11. Supplementary Notes. Enter information not included elsewhere such as: Prepared in cooperation with...; Trans. of...; To be published in.... When a report is revised, include a statement whether the new report supersedes or supplements the older report.

Block 12a. Distribution/Availability Statement. Denotes public availability or limitations. Cite any availability to the public. Enter additional limitations or special markings in all capitals (e.g. NOFORN, REL, ITAR).

- **DOD** - See DoDD 5230.24, "Distribution Statements on Technical Documents."
- **DOE** - See authorities.
- **NASA** - See Handbook NHB 2200.2.
- **NTIS** - Leave blank.

Block 12b. Distribution Code.

- **DOD** - Leave blank.
- **DOE** - Enter DOE distribution categories from the Standard Distribution for Unclassified Scientific and Technical Reports.
- **NASA** - Leave blank.
- **NTIS** - Leave blank.

Block 13. Abstract. Include a brief *(Maximum 200 words)* factual summary of the most significant information contained in the report.

Block 14. Subject Terms. Keywords or phrases identifying major subjects in the report.

Block 15. Number of Pages. Enter the total number of pages.

Block 16. Price Code. Enter appropriate price code *(NTIS only)*.

Blocks 17. - 19. Security Classifications. Self-explanatory. Enter U.S. Security Classification in accordance with U.S. Security Regulations (i.e., UNCLASSIFIED). If form contains classified information, stamp classification on the top and bottom of the page.

Block 20. Limitation of Abstract. This block must be completed to assign a limitation to the abstract. Enter either UL (unlimited) or SAR (same as report). An entry in this block is necessary if the abstract is to be limited. If blank, the abstract is assumed to be unlimited.

*U.S.GPO:1993-0-358-779

FOREWORD

Opinions, interpretations, conclusions and recommendations are those of the author and are not necessarily endorsed by the US Army.

____ Where copyrighted material is quoted, permission has been obtained to use such material.

____ Where material from documents designated for limited distribution is quoted, permission has been obtained to use the material.

VBH Citations of commercial organizations and trade names in this report do not constitute an official Department of Army endorsement or approval of the products or services of these organizations.

____ In conducting research using animals, the investigator(s) adhered to the "Guide for the Care and Use of Laboratory Animals," prepared by the Committee on Care and Use of Laboratory Animals of the Institute of Laboratory Resources, National Research Council (NIH Publication No. 86-23, Revised 1985).

VBH For the protection of human subjects, the investigator(s) adhered to policies of applicable Federal Law 45 CFR 46.

____ In conducting research utilizing recombinant DNA technology, the investigator(s) adhered to current guidelines promulgated by the National Institutes of Health.

____ In the conduct of research utilizing recombinant DNA, the investigator(s) adhered to the NIH Guidelines for Research Involving Recombinant DNA Molecules.

____ In the conduct of research involving hazardous organisms, the investigator(s) adhered to the CDC-NIH Guide for Biosafety in Microbiological and Biomedical Laboratories.

Vincent B. Ho 12 Sept 96

PI - Signature Date

I. Table of Contents

Front Cover	Page 1
SF 298	Page 2
Foreword	Page 3
Table of Contents	Page 4
Introduction	Page 5
Body	Page 7
Conclusion	Page 12
References	Page 13
Figures	Page 14
List of Publications	Page 15
List of Personnel	Page 15

II. Introduction

Background

Despite the dramatic improvements in breast cancer detection programs in recent years, the overall and age-adjusted incidence rates for breast cancer have gradually increased 1-2 percent a year [1,2]. Magnetic resonance mammography (MRM) is potentially a very powerful adjunct in breast cancer detection and surveillance [3-16]. Initial studies, mainly performed in Germany, have reported MRM to have the ability to detect malignant breast lesions and to successfully distinguish malignant from benign breast disease with high diagnostic accuracy (70-90%) [3-16]. Dr. Werner Kaiser, who has the largest world-wide experience of over 2,100 cases, reports MRM to have a diagnostic accuracy of 97.1% for breast cancer with sensitivity of 97.3% and specificity of 96.9% (personal communication, November 1993).

Magnetic resonance (MR), although not utilizing ionizing radiation, can identify breast cancer based on its preferential enhancement following the intravenous administration of gadolinium(Gd)-chelate contrast media. The identification of Gd-enhancement is most dramatic on T1-weighted MR sequences and is visualized as bright signal intensity. Fat, however, on T1-weighted MR images is also bright. The identification of Gd-enhancement on MR is, thus, hindered in regions with abundant fat -- this is especially true in MR of the breast. Subtle areas of bright Gd contrast enhancement may thus be imperceptible in areas of predominantly similarly bright fatty tissue.

The conspicuousness of Gd-enhancement can be overcome by one of two general MR techniques [3-16]. The first [6] utilizes image subtraction whereby pre-contrast images (fat is bright, tumor is dark as it has not been enhanced) are subtracted from post-contrast images (both fat and the tumor are bright). Theoretically, this technique will result in the depiction of only the enhancing regions. This technique, however, is not without error as even the most minute patient motion during the examination or variation in image acquisition will result in misregistration of pre- and post-contrast image slices. This, in turn, will yield a suboptimal, artifact-plagued subtracted image which may result in the rendering of erroneous interpretations.

The second method, utilized to increase the conspicuousness of contrast-enhancement on MR entails the use of a fat suppression technique [5,12,13]. Standard commercially available fat suppression techniques, however, are far from ideal and are frequently incomplete. This is particularly true of breast MR, where the use of the conventional fat suppression technique (FATSAT) often results in inadequate and inhomogeneous fat suppression. Conventionally fat-suppressed images are frequently artifact plagued and of poor quality which directly affects the study's diagnostic accuracy. This often results in the performance of repeat T1-weighted images and the prolongation of examinations.

Phase unwrapping in the 3-point-Dixon (PU3PD) method is a recently described alternative method for fat suppression which promises to bridge the difficulties encountered with fat signal on post-contrast MRM images. This new fat suppression

technique was developed by Szumowski et al. in 1994 [17] and promises to provide the reproducible homogeneous fat suppression necessary for the efficient performance of MRM and the accurate rendering of diagnoses.

This new technique, by increasing the conspicuousness for areas of Gd-enhancement, promises to dramatically improve the overall accuracy of MRM for breast cancer and make the identification of even very small cancers possible. MR with its reported high sensitivity will potentially identify lesions not otherwise detected by film screen mammography, ultrasound or physical exam. Because the success of any breast imaging modality relies on its ability to diagnose cancer early to effect cure and increased survival, this technique promises to be a major advance in breast cancer imaging.

Objectives

The objectives of this protocol ("Magnetic Resonance Mammography (MRM): A Promising Application for Fat Suppression by Phase Unwrapping in the 3-Point-Dixon Method) was (1) to further refine the fat suppression technique utilizing phase unwrapping in a 3-point-Dixon method as originally described by Szumowski et al. [17] for application on a version 5.x General Electric (GE) Signa 1.5 Tesla MR scanner and (2) to compare the PU3PD technique with other forms of conventional techniques for fat signal elimination, subtraction 3D SPGR and FATSAT, in magnetic resonance mammography (MRM).

Hypothesis

The use of phase unwrapping in a 3-point-Dixon method for achieving fat suppression will dramatically improve the ability of MRM to detect enhancing breast lesions over conventional fat suppression techniques (subtraction 3D SPGR and FATSAT).

III. Body

Protocol Status

Parts I and III (5 December 1994 - 1 September 1995)

[Note that Part II, the initiation of the clinical MRM portion of the project, was postponed pending the upgrade of Madigan's MR scanner to version 5.X of the MAMC GE MR scanner. The initiation of the clinical trial was delayed so that the data collection (all performed at the version 5.x software level) would not be affected by a change in operating systems midway. A prolonged delay in the delivery of the 5.x upgrade to the MAMC MR scanner resulted from expiration in the federal contract with GE for 5.x upgrades which was army wide. Consequently, an extension was requested and approved from MAJ Friedl of the USMRMC for the completion of Parts II and IV]

Further refinement and development of PU3PD technique was performed by the Radiology Imaging Research Laboratory at the Oregon Health Sciences University (OHSU) in Portland, Oregon, under the supervision of Dr. Jerzy Szumowski. [1] The technique, originally developed for a version 4.x GE MR scanner, was revised to be performed on a version 5.x GE MR scanner *[Part III of the protocol]* which has a markedly different hardware and software environment from its older version 4.x generation.. This change in the PU3PD algorithm necessitated the revision and re-implementation of the pulse sequence code using a new compiler. The development of the new PU3PD algorithm was performed at OHSU's version 5.x GE 1.5 Tesla MR scanner. In addition, the scanning time in the refined technique was further reduced by 50% by improvements in the original software design. The 50% reduction of the imaging time affords improved temporal resolution required for time vs. signal intensity evaluations. There is clearly a time-related variable to the enhancement of malignant breast tumors versus benign masses [3-16]. Malignant breast tumors typically enhance earlier and more intensely than benign breast masses.

At OHSU, testing of the refined PU3PD technique on phantoms occurred during May and June 1995 and on a small series of volunteers at OHSU in early June 1995. The tests have confirmed adequate fat and water signal separation, adequate fat signal elimination and spatial uniformity. Although the technique could have been ready for implementation at Madigan Army Medical Center (MAMC) earlier, MAMC's MR scanner had not yet been upgraded to the version 5.x. The added time, however, allowed for further fine tuning of the technique at OHSU. The initial timeline for the protocol had estimated a late Winter/Spring 1995 delivery for the upgrade of MAMC's MR scanner. However, due to a number of official and contractual changes, the upgrade of the MAMC MR scanner to version 5.x was rescheduled for delivery in August 1995.

[1] Priot to the initiation of the project, research agreements were established between MAMC and OHSU as well as between MAMC and GE Medical.

Paralleling the revision of the PU3PD algorithm for the version 5.x GE MR scanner, the Radiology Imaging Research Laboratory OHSU, again under the supervision of Dr. Jerzy Szumowski, has been testing new interfaces on a SUN SPARC workstation for the post-acquisition processing and image reconstruction of the MR raw data obtained by the PU3PD technique. The technique was further refined for processing in the Advance Visualization System (AVS) software environment.

Parts II and IV (1 September 1995 - 1 June 1996)

Following the upgrade of the MAMC GE MR scanner to version 5.x in late August 1995, the refined version of PU3PD developed at OHSU *[Part III]* was loaded onto the GE MR scanner at Madigan Army Medical Center by Dr. Szumowski and the OHSU team. Acceptance testing of the PU3PD algorithm with a variety of test phantoms was performed and resulted in successful image acquisitions. The MAMC MR technologists were trained by the OHSU team to perform the PU3PD technique and to process data on the MAMC GE SUN SPARC AW workstation. Clinical trials at MAMC began 15 September 1996.

Subjects:

Between 15 September and 1 April 1996, 17 female patients (ages 32-74 years; mean = 48.76 years) enrolled in the study. In all patients, MRM was performed as an adjunct to the evaluation of a suspicious mammographic finding [mass (n=11), indeterminate cluster of microcalcifications (n=6), architectural distortion (n=1)] which was scheduled for surgical or stereotactic breast biopsy. In one patient, suspicious mammographic abnormalities were noted in both breasts and two separate MRM examinations were performed, one for each breast. Informed consent was obtained in all patients.

Materials and Methods:

The original 1994 protocol, was designed to compare the gadolinium (Gd)-enhanced MRM images using the PU3PD technique to that using conventional FATSAT based on a 2-dimensional spin-echo T1-weighted MR sequence. However, more recent articles on MRM [18-22] had shown the use of a subtraction 3-dimensional spoiled gradient-echo (3D SPGR) technique preferable for MRM as it provided both improved spatial and temporal resolution to that of FATSAT spin-echo T1-weighted images. Specifically, the T1-weighted images required slice gaps whereas 3D SPGR images could provide higher resolution contiguous data sets and the FATSAT T1-weighted images required a much longer acquisition time. Based on these newer studies, the MRM protocol of this project was augmented to incorporate a comparison with the reportedly better 3D SPGR MRM technique.

In addition, most academic breast centers including the one at MAMC have shifted their role of MRM from a "screening" to that of a "problem-solving" tool. This

paradigm shift has been due to a variety of factors which include the absence of a good MRM technique for bilateral breast imaging, the cost for MRM and the diagnostic dilemmas created by the MRM identification of unsuspected abnormalities remote to area of concern, especially those in the contralateral breast. With this changing emphasis to "problem-solving," the MRM protocol for this study was redesigned with "screening" as only a secondary goal.

In the revised study plan, unilateral 3D SPGR [25/8.4/50^0/2; repetition time (TR)/echo time (TE)/flip angle (FA)/excitations (NEX)] and unilateral PU3PD images were obtained immediately following intravenous Gd-chelate contrast media administration to afford the best temporal resolution. The imaging of only the breast with the mammographic suspicious region allowed for improved spatial resolution as the field of view (16-24cm) could be limited to the breast in question. Both the 3D SPGR technique, which utilized image subtraction of pre-contrast from post-contrast images for fat elimination, and the PU3PD T1-weighted images were performed with nearly similar imaging parameters (slice locations, matrix (256x128 matrix), slice thickness (2 mm), etc.) and both required roughly the same amount of imaging time (approximately 3 1/2 minutes). The acquisition of the 3D SPGR images and the PU3PD images were randomized following the intravenous bolus administration of 0.15 mmol/kg of Gadolinium-chelate contrast media in an effort to minimize temporal bias between the techniques for lesion enhancement. In addition, an intravenous catheter was placed in an antecubital vein prior to the MRM examination to minimize patient motion which may occur between imaging sequences. This was particularly important for more accurate subtraction of the 3D SPGR images. Each Gd-chelate contrast media bolus was also followed by an intravenous bolus of 10 ml sterile saline to ensure that the complete Gd-chelate dose was administered.

The FATSAT and PU3PD T1-weighted images [500-800/16-40/2; TR/TE/NEX] were performed approximately 10-15 minutes following contrast administration. Because FATSAT is highly sensitive to the homogeneity of the magnetic field, the FATSAT/PU3PD comparison was performed of both breasts over a large field of view (28-36 cm), accentuating the differences in fat signal elimination between the two techniques. This bilateral breast imaging also afforded the testing of the PU3PD technique for potential use as a "screening" examination. The FATSAT and PU3PD images were matched in their image parameters (256x128 matrix, 4 mm slice thickness) and prescriptions, just as the 3D SPGR and PU3PD images were.

Prior to the initiation of the clinical trial, the investigators decided to defer all clinical decisions on previously unsuspected "suspicious" breast lesions which were identified on MRM to clinical judgments based on review of conventional mammographic and/or sonographic examinations on a case by case basis. In addition, all available mammographic studies (film screen and/or ultrasound) were reviewed prior to each MRM examination.

In total, 18 MRM examinations were performed on the 17 participants in this study. MRM examinations were performed using a 1.5 Tesla GE Signa version 5.4 MR scanner and a dedicated GE breast coil. The breasts of each patient were padded to

minimize motion while positioned prone in the breast coil. All 18 MRM examinations included matching pre- and post-contrast 3D SPGR and PU3PD images. Eleven of the MRM examinations included post-contrast PU3PD and FATSAT T1-weighted images. In 7 patients, either time limitations, patient discomfort or technical malfunctions precluded the acquisition of the FATSAT and/or PU3PD T1-weighted spin-echo images. Several actual defects in two or more MRI scanner hardware components were discovered during the course of the study which had resulted in the inability to obtain T1-weighted spin-echo images while in the research mode.

Data Collection:

Up to 4 sets of MRM images were obtained for each patient, two sets for each comparison of 3D SPGR/PU3PD and FATSAT/PU3PD. Each set of MRM images was prospectively interpreted . Each set of 3D SPGR subtraction images and FATSAT images was also compared to their corresponding set of PU3PD images. Images were interpreted qualitatively in terms of their (1) fat elimination and (2) characterization of mammographically suspicious region or lesion. The grading scale was: [1] - PU3PD better; [2] - same; [3] - 3D SPGR or FATSAT better. All image interpretations were performed with conventional mammographic studies available, as would be the clinical scenario of a "problem-solving" MRM. All film interpretations were performed with availability of the patient's film screen mammograms and/or ultrasound images without knowledge of pathologic diagnosis.

All pathologically proven breast lesions were characterized in terms of their enhancement pattern and morphologic features on each of the 3D SPGR/PU3PD and FATSAT/PU3PD pairings. All enhancing lesions were assessed for degree of enhancement qualitatively on an independent computer workstation using operator defined regions-of-interest on the pre- and post-contrast 3D SPGR images.

Results:

Each pairing of MRM were prospectively evaluated in terms of overall fat signal elimination on the post-processed images and of MRM depiction of the suspicious region or "lesion" which had been the reason for the patient's referral.

Fat Elimination:

1. 3D SPGR versus PU3PD. In 16/18 (89%) cases, the PU3PD method of fat signal elimination was preferred to that of 3D SPGR subtraction; in 2/18 (11%) cases the elimination methods were found to be the same. The subtraction of 3D SPGR images resulted in subtraction artifact in most cases especially along the surface of the skin secondary to patient motion during the interval between sequences.
2. FATSAT versus PU3PD. In 8/11 (73%) cases, the PU3PD method of fat signal elimination was preferred to that of FATSAT; in 3/11 (27%) cases, the elimination methods were thought to be the same.

Mammographically Suspicious Region/Lesion Depiction:

1. 3D SPGR versus PU3PD. In 16/18 (89%) cases, the PU3PD method of fat signal elimination was preferred to that of 3D SPGR subtraction for the delineation of the suspicious region/lesion; in 2/18 (11%) cases the elimination methods were found to be the same.
2. FATSAT versus PU3PD. In 6/11 (55%) cases, the PU3PD method of fat signal elimination was preferred to that of FATSAT for the depiction of the suspicious region or lesion; in 5/11 (45%) cases, the elimination methods were thought to be the same.

Pathologic confirmation was available in 15 [ductal hyperplasia (n=4); infiltrating ductal carcinoma (n=3); fibroadenoma (n=3); lobular hyperplasia (n=2); epithelial hyperplasia (n=1); fibrosis/elastosis (n=1); and fat necrosis (n=1)] of the 18 suspicious mammographic lesions. Seven (3/3 infiltrating ductal carcinoma, 3/3 fibroadenoma, 1/1 epithelial hyperplasia; 9-30 mm , average = 14.4 mm) of the 15 lesions were noted to significantly enhance on MRM *[enhancement was defined as 100% change in signal intensity on 3D SPGR images following the administration of Gd-chelate contrast media].* Lesion enhancement was noted on every sequence (3D SPGR, FATSAT and PU3PD) when it was present. In each case, lesion enhancement was dramatic (>>100%). Region of interest analysis of pre- and post-contrast 3D SPGR images revealed dramatic (200-500%) enhancement in all cases; however, no distinguishing threshold of enhancement was identified which separated benign from malignant histology (fibroadenomas were noted to enhance just as brightly as the infiltrating ductal carcinomas). All three infiltrating ductal carcinomas were noted to be poorly marginated which corresponded to their spiculated appearance on film screen mammogram. One infiltrating ductal carcinoma was noted to have "ring" enhancement. Two of the three fibroadenomas were noted to be well circumscribed and lobular in their margins. The remaining fibroadenoma had slightly less well-defined margins but was small (9 mm) embedded in dense mildly enhancing glandular tissue. In two of the fibroadenomas, septations were evident. The remaining lesion containing epithelial hyperplasia was well-circumscribed and homogeneously and brightly enhancing. In 4/7 enhancing lesions the PU3PD images better delineated the characteristics of the lesion than the subtraction 3D SPGR images; in 3/7, the images were the same. In all cases in which the PU3PD images were preferred, the 3D SPGR subtraction was suboptimal and had resulted in suboptimal blurring of the lesion and artifactual generation of artifact. In one case, the superficial margin of the enhancing lesion could not be distinguished from the skin surface. FATSAT/PU3PD T1-weighted images were available on only four lesions; however, they were similar in their characterization of the lesions which was fair overall.

III. Conclusions

In this pilot study, 18 women with suspected breast pathology were imaged using a variety of conventional (3D SPGR and FATSAT) and research (PU3PD) MRM techniques utilizing a version 5.4 GE Signa 1.5 Tesla MRI scanner. The PU3PD was found to be preferable for fat signal elimination in most cases when compared with that of subtraction 3D SPGR. The use of the 3D SPGR subtraction technique was hampered by imprecise subtraction of images which resulted in artifactual bright regions which was especially evident along the surface of the breast and in one case obscured the superficial margin of an invasive carcinoma. Overall, the edges of the enhancing lesions were best depicted on the PU3PD images.

Characterization of the internal and external morphology of the enhancing lesions was better on the PU3PD images. However, no distinctive degree of enhancement was associated with benignity or malignancy which correlates with the reported overlap of enhancement [20-22]. This was particularly true in our study possibly because of our acquisition times of 3-4 minutes with both the 3D SPGR and PU3PD. The degree of enhancement, furthermore, is probably more dependent on the density and distribution of microvessels than actual benign or malignant histology [23]. All three malignant lesions enhanced significantly on all the sequences, but notably on the PU3PD images as well. Several previously reported features of benign and malignant lesions were also seen in the study ("ring" enhancement, a sign for malignancy and "septations" a sign for fibroadenoma).

The comparison of FATSAT with PU3PD was suboptimal secondary to a number of factors, most notably the delay in their acquisition relative to the gadolinium-chelate contrast media administration. In addition, the enlargement of the field of view to accomodate bilateral MRM and the need for thicker (slices were 4 mm which was twice that of the unilateral 3D SPGR and PU3PD exams) slices for coverage of the breasts resulted in decreased spatial resolution. Use of a faster and higher resolution method for bilateral breast imaging will probably be necessary for MRM to be an effective screening tool. The PU3PD, in any case, afforded excellent fat signal elimination which was same or better than FATSAT in all cases.

Currently, a quicker method of image acquisition of the PU3PD technique using a 3D SPGR rather than a T1-weighted sequence as was used in this study is being developed. A 3D SPGR version of the PU3PD technique may supply the temporal resolution necessary to better differentiate benign from malignant lesions -- thereby improving the specificity of lesion characterization based on their enhancement over time. A 3D SPGR version of the PU3PD technique hopes to offer the advantage of faster, high resolution 3D imaging without the subtraction artifacts of image subtraction or time requirements of FATSAT and T1-weighted imaging.

In conclusion, PU3PD is a new MRM technique which promises to outperform the conventional methods (subtraction 3D SPGR and FATSAT) of fat signal elimination for MRM. This technique has been developed for application using a T1-weighted spin echo sequence on a version 5.4 GE Signa 1.5 Tesla MRI scanner.

References

[1] Miller BA, Feuer EJ, Hankey BF. Recent incidence trends for breast cancer in women and relevance of early detection: An Update. CA 1993;43:27-41

[2] Harrris JR, Lippman ME, Veronsesi U, et al. Breast cancer (Part 1). N Engl J Med 1992;327:319-328

[3] Kaiser WA, Zeitler E. MR imaging of the breast: Fast imaging sequences with and without Gd-DTPA. Radiology 1989;170:681-686

[4] Stack JP, Redmond OM, Codd MB, et al. Breast disease: Tissue characterization with Gd-DTPA enhancement profiles. Radiology 1990;174:491-494

[5] Pierce WB, Harms SE, Flamig DP, et al. Three-dimensional gadolinium-enhanced MR imaging of the breast: Pulse sequences with fat suppression and magnetization transfer contrast. Work in progress. Radiology 1991;181:757-763

[6] Gilles R, Guinebretiere J-M, Shapeero LG, et al. Assessment of breast cancer recurrence with contrast-enhanced subtraction MR imaging: Preliminary results in 26 patients. Radiology 1993;188:473-478

[7] Kaiser WA. MRM promises earlier breast cancer diagnosis. Diagnostic Imaging 1992;88-93

[8] Heywang SH, Wolf A, Pruss E, et al. MR imaging of the breast with Gd-DTPA: Use and limitations. Radiology 1989;171:95-103

[9] Heywang SH, Hibertz T, Beck R, et al. Gd-DTPA enhanced MR imaging of the breast in patients with post-operative scarring and silicon implants. J Comput Assist Tomogr 1990;14:348-356

[10] Harms SE, Flamig DP. MR imaging of the breast: Technical approach and clinical experience. RadioGraphics 1993;13:905-912

[11] Harms SE, Flamig DP. Present and future role of MR imaging. In: Haus AG and Yaffe MJ (eds.) Syllabus. A categorical course in physics: Technical aspects of breast imaging. Oakbrook, IL: RSNA Publications, 1992

[12] Harms SE, Flamig DP, Hesley KL, et al. Fat-suppressed three-dimensional MR imaging of the breast. RadioGraphics 1993;13:247-267

[13] Whitney W, Herfkens RJ, Silverman J, et al. Gadolinium-enhanced spectral-spatial MRI for evaluation of breast carcinoma (abst.). Society of Magnetic Resonance in Medicine annual meeting, New York 1993

[14] Weisskoff RM, Hulka CA, Smith B, et al. Dynamic NMR imaging of the breast using echo planar imaging (abst.). Society of Magnetic Resonance in Medicine annual meeting, New York 1993

[15] Turner DA, Wang JZ, Economou SG, et al. Functional images from dynamic, contrast-enhanced 2DFT MR images for the detection of breast cancer (abst.). Society of Magnetic Resonance in Medicine annual meeting, New York 1993

[16] Hess T, Knopp MV, Brix G, et al. Pharmacokinetic mapping of breast lesions by dynamic Gd-DTPA enhanced MRI (abst.). Society of Magnetic Resonance in Medicine annual meeting, New York 1993

[17] Szumowski J, Coshow WR, Li F, Quinn SF. Phase unwrapping in the Three-Point Dixon method for fat suppression MR imaging. Radiology 1994;192:555-561

[18] Heywang KSH. Contrast-enhanced magnetic resonance imaging of the breast. Invest Radiol 1994;29:94-104

[19] Weinreb JC, Newstead G. MR imaging of the breast. Radiology 1995;196:593-610

[20] Kerslake RW, Carleton PJ, Fox JN, et al. Dynamic gradient-echo and fat-suppressed spin-echo contrast enhanced MRI of the breast. Clin Radiol 1995;50:440-454

[21] Orel SG, Schnall MD, LiVolsi VA, Troupin RH. Suspicious breast lesions: MR imaging with radiologic-pathologic correlation. Radiology 1994;190:485-493

[22] Fobben ES, Rubin CZ, Kalisher L, Dembner AG, Seltzer MH, Santoro EJ. Breast MR imaging with commercially available techniques: radiologic-pathologic correlation. Radiology 1995;196:143-152

[23] Buada LD, Murakami J, Murayama S, et al. Breast lesions: Correlation of contrast media enhancement patterns on MR images with histopathologic findings and tumor angiogenesis. Radiology 1996;200:639-649

List of Publications:

Ho VB, Szumowski J, Youngberg RA. "Magnetic Resonance Mammography (MRM): A Promising Application for Fat Suppression by Phase Unwrapping in the 3-Point-Dixon Method" (in preparation)

List of Personnel:

Principal Investigator:

MAJ Vincent B. Ho, MC, USAR - Madigan Army Medical Center (no pay received)

Associate Investigators:

Rush A. Youngberg, M.D. - Madigan Army Medical Center (no pay received)
Jerzy Szumowski, Ph.D. - Oregon Health Sciences University

Technical Staff:

William Coshow, M.S. - Oregon Health Sciences University
Fang Li, M.S. - Oregon Health Sciences University

Clinical Coordinator:

Maureen N. Kistler, BS, RT(MR) - Madigan Army Medical Center