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Final Interim Report
Candidate Sites, Machines in Use, Data Storage and Transmission Methods

Testing Feasibility of 3-D Ultrasound Data Acquisition and Reliability of Data Retrieval from Stored 3-D Images

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Deliverable for Task 02 of Work Assignment 02-03

Candidate Sites, Machines in Use, and Data Storage and Transmission Methods

1.0 Introduction

The purpose of this Work Assignment, 02-03, is to examine the feasibility of collecting, transmitting, and analyzing 3-D ultrasound data in the context of a multi-center study of pregnant women. The study will also examine the reliability of measurements obtained from 3-D images that have been stored and retrieved.

The first deliverable under this assignment was the creation of a work plan that outlined the tasks, schedule, deliverables, and budget. This was submitted to EPA on February 12, 2004. The second deliverable for the work assignment was the interim report. A draft of the interim report, including a description of candidate sites and the machines in use at these sites as well as the file storage and transmission options was submitted to EPA. The draft interim report listed the steps that would be taken by RTI to complete the site selection process and the file storage and transfer method determination. This document, the final interim report, includes our assessment of and recommendations for data including 3-D volume datasets, storage, transfer and retrieval, as well as potential local sites and central facility.

A brief background of the study and detailed information about individual components that are appropriate for review is presented below.

2.0 Background

The expectation of the work assignment is that it will provide the NCS planners the information necessary to decide on the feasibility of including 3-D organ volume measurements to the antenatal assessment protocol. The work assignment will determine whether it is feasible to uniformly collect 3-D fetal organ volume measurements from multiple centers across the U.S. and then transmit the data to a central location, where the data can be analyzed to reliably assess

fetal growth and development. Potentially, these sites will be using different 3-D obstetrical ultrasound machines. The questions being asked are:

- Can sonographers visualize and obtain a volume measurement, using their 3-D ultrasound machines, of the fetal head, heart, kidneys, adrenal glands, lungs, pancreas, liver, upper arms, and thighs?
- Can "raw" 3-D data be saved, transferred, and stored at a central facility without losing the quality of the images/data?
- Can the stored "raw" 3-D data be brought back into software that will allow an ultrasound interpreter (sonographer or MD) to view, manipulate, and determine volumes of organs? Is there a standard software package that can read data obtained from different models and brands of ultrasound machines?
- What is the burden on a site and a patient of obtaining 3-D volumes ("raw data") during the exam, determining organ volume measurements after the exam, and saving and storing the 3-D "raw" data for later analysis by the Central Facility?
- Will different sonographers at the central facility arrive at the same organ volume measurements when viewing the same "raw" 3-D data?

Planning for the National Children's Study (NCS) includes planning for the measurement of growth of the fetus both as a pregnancy outcome and in relation to potential influences on health later in life. One method of evaluating fetal growth and integrity is through an ultrasound exam. An ultrasound exam involves sending high-frequency sound waves into a woman's uterus from a transducer resting on the woman's abdomen. The sound is reflected off the fetus and fetal internal structures and the returning echoes are received by the transducer and converted by an electronic instrument into an image of the fetus and its internal structures on the monitor. While 2-D ultrasound imaging has become an established tool for obstetricians across the United Stated, 3-D ultrasound imaging is a relatively new yet promising technology. 3-D ultrasound has several potential advantages over traditional 2-D imaging, including volumetric and morphologic information on organs and structural elements of the fetus and the fetal-placental unit, many of which cannot be obtained with 2-D ultrasound. A 3-D rendering of an organ or structure provides the physician, or researcher, information to evaluate the growth, development and

morphologic abnormalities of critical structures and organs such as the skeleton, structures in the brain, heart, kidneys, and adrenal glands. The ability to retrieve stored images and make measurements after the scan could allow for a rich dataset for future analyses.

The technology supporting 3-D (and 4-D) ultrasound is advancing rapidly. The question being addressed by this work assignment is whether 3-D has progressed to a point that 3-D obstetrical ultrasound data can be uniformly collected from multiple centers, transported to a central location, and then used to assess fetal growth and development. Although this work assignment focuses on the feasibility of using 2-D and 3-D ultrasound measurements in the NCS, 4-D ultrasound has been introduced and may become widely used. 4-D is the ability to view 3-D images in real time, allowing for the movement of 3-D images.

The first step in determining the feasibility of collecting, transmitting, and analyzing 3-D ultrasound data in the context of a multi-center study of pregnant women is locating potential sites and evaluating their 3-D obstetrical ultrasound machines and their storage and transfer options. The limitations and advantages of the machines and storage and transfer options are necessary to determine the preferred transfer mechanism for the pilot.

3.0 Potential Sites

RTI developed a set of site criteria as a way to evaluate potential institutions. Meeting these criteria increases the likelihood that a site will be able to meet the rigorous timeline and protocols. The criteria are:

- The medical center meets the AIUM (American Institute of Ultrasound in Medicine) ultrasound standards and guidelines and are currently using 3-D ultrasounds for antenatal assessment
- The sonographers performing the study ultrasound exams are ARDMS (American Registry of Diagnostic Medical Sonographers) certified and have 3-D ultrasound experience
- The sonographers are not MDs (as is anticipated for the NCS due to cost)

- The sonographer who performs the exam will determine the organ volume measurements once the patient has left
- The site has experience working with their institution's IRB (Institutional Review Board)
- The study personnel have computer support on-site
- All study exams can be performed on a GE Voluson 730
- The volume of patients in the clinic allow data to be collected within 1-2 months
- The study personnel have previous research experience

RTI, with input from EPA, decided that it would be ideal if the following criteria were met by at least one site:

- The ability to transfer the 3-D volume datasets directly from the GE Voluson 730
- 3-D volume organ measurement experience
- Access to, and been trained to use, the Philips iu22 ultrasound machine

Discussions with potential sites resulted in insight into the current knowledge about 3-D ultrasound and the areas that are being explored. All potential sites listed below are aware that being in this feasibility study does not in any way affect their chances to be a site in the NCS. In addition, the data will belong to the EPA and any rights to publish from the data will be EPA's prerogative.

From the institutions contacted, and the discussions with Dr. Chris Macedonia, it appears that the GE Voluson 730, and possibly the IU22 Philips machine, is the only 3-D OB ultrasound machine with the technical advancements necessary to accurately and consistently visualize and determine organ volume measurements.

The contacts at GE and Philips and Dr. Chris Macedonia agree that future machines will be even better than the GE Voluson 730 and Philips IU22.

RTI contacted sales and technical representatives from GE, manufacturer of the Voluson 730, to discuss data transmission, storage, and retrieval of 3-D volume datasets. We were told that 3-D images are stored in a proprietary format on the ultrasound machine and must be viewed and analyzed either on the ultrasound machine or on a personal computer using GE's 4D View 2000 software. GE staff indicated that 3-D is in its early stages and the technology is changing quickly. Since there are no standards, companies are moving ahead with their proprietary solutions. GE representatives said that they think there will be a standard in the next 2 – 3 years. The files containing 3-D images can range in size from 10 Mb to 100 Mb or more. (Potential sites have indicated that the size may be more like 50 Mb to 170 Mb.) There currently is no accepted compression technique for compressing the 3-D images natively. GE staff said that, at the current time, CD/DVD is the best way to transmit 3-D images because of the expected file sizes.

Dr. Chris Macedonia alerted us to the fact that Philips would be releasing a new 3-D machine that would be able to perform at least as well as the GE Voluson 730 and gave us a Philips representative to contact. According to the Philips sales representative, the IU22 was released on February 12, 2004. The GE representative said that the new machine is able to perform all of the functions of the GE Voluson 730. The advances made in the 2-D imaging resolution are said to be significant, which can only increase the resolution of the 3-D images. In addition, it requires little manipulation such as the "gain" or "brightness" by the sonographer to obtain the best image. While having two different ultrasound machines might be beneficial to the pilot, the Philip's IU22 machine has had reliability issues when used by Dr. Delores Pretorius, a leader in the field of 3-D fetal imaging. Perhaps a separate study of the validity of the Philips IU22 as compared to the GE Voluson 730 is necessary before utilizing the machine in the feasibility pilot.

3.1 Candidate 1: Duke University

Duke's OB Ultrasound department meets the criteria for a site. They currently use 3-D to confirm 2-D findings and to enhance bonding. At present, they do not obtain organ volumes as part of a routine exam but at least one physician is experienced in obtaining 3-D volumes and

determining 3-D organ volume measurements. They anticipate a need to be reimbursed for their sonographer's time at $441 per completed patient.

An advantage to this site is their great interest in the study and, therefore, giving it priority in the IRB process and data collection. In addition, their location being within 30 minutes from RTI would allow easy travel for training or support during data collection.

3.2 Candidate 2: Naval Medical Hospital in San Diego

The Naval Medical Ultrasound department meets the criteria for a site. They currently use their GE Voluson 730 to perform 2-D and 3-D exams. In most clinical exams, 3-D is used to confirm 2-D findings and to enhance bonding. This potential site is also using the GE Voluson 730 to collect 3-D volumes as part of a research project. They anticipate a need to be reimbursed for their sonographer's time at $170 per completed patient.

An advantage to this site is that Dr. Linda Chan's current research study, looking at 3-D volumes of 1st trimester fetuses collected on Naval ships at sea and interpreted on land, has met with acceptance by her department as well as her IRB. During preliminary discussions with her IRB, neither she nor her IRB anticipate difficulty obtaining approval if they are chosen to be a site. In addition, Dr. Linda Chan has the experience with training on 3-D volume acquisition and has created training materials that she has offered to the used for this feasibility study. Another advantage to this site is that the computer and internet support personnel are available to try to transmit 3-D volume datasets directly from the GE Voluson 730, if this is desired.

3.3 Candidate 3: University of California at San Diego

Dr. Delores Pretorius and her staff at the University of California at San Diego meet the criteria for a site. They anticipate a need to be reimbursed for their sonographer's time at $300-$500 per completed patient and $7,000-$10,000 for study-related oversight, coordination, and related functions.

An advantage of this medical center is that Dr. Pretorius has been a pioneer in the field of 3-D ultrasound. She has written articles with Dr. Wesley Lee and Dr. Thomas Nelson on many different aspects of 3-D ultrasound and organ volume measurements from the 3-D volume datasets. The feasibility study would benefit by insights gained from her knowledge and assistance.

The medical center uses the GE Voluson 730, and has just received a Philips IU22. Having a single site with both machines would enable a comparison across machines using the same sonographers, if desired.

This site also has the expertise and oversight necessary to perform the additional responsibility of being the Central Facility. Two sonographers, other than those who perform the study exams and organ volume measurements, are available to review and determine organ volume measurements from the stored 3-D volume datasets.

3.4 Candidate 4: University of North Carolina at Chapel Hill (UNC-CH)

UNC-CH's Obstetrical Department uses the GE Voluson 730 for 3-D organ volume measurement. Their interest has been continuous throughout the study development, however, a final cost has yet to be obtained and is the only reason they are listed here as a fourth alternative.

One possible advantage for this site is that they would use the same IRB as the EPA. There is a possibility therefore that the site approval process could be granted in a short time period.

Dr. Tom Trevitt, who would most likely oversee the feasibility study at UNC if they are chosen to be a site, is involved in a 3-D organ volume measurement project. While his protocol for obtaining a 3-D volume and determining organ volume measurements differs from the one proposed for this study, he is confident that his sonographers could follow the protocol as proposed.

4.0 Data Transmission to the Central Facility

RTI considered a number of methods of transmitting files containing 3-D volumes from the sites to the Central Facility. RTI considered factors such as availability of high speed connections, security of the transmission, amount of time required to transmit files containing 3-D volumes, reliability of the transmission, availability of workstations at the sites for uploading data, burden on the sonographer, etc.

We searched the Internet to gather information on how other organizations transmit large files hoping to find a method that was secure, reliable, fast, etc. We learned that a large file is defined as 10 – 30 Mb. Whereas, this study is expecting to transmit file sizes from 50 Mb to 170 Mb or larger. Consequently, the files we want to transmit can probably not be transmitted using methods normally used.

We established a web site to test uploading large files. RTI has a DS3 (digital T3) connection to the Internet that enables uploading at approximately 4.5 Mbs (megabytes per second). We were able to upload files with sizes up to 70 Mb with few problems, but were not able to upload larger files.

It took approximately 15 minutes to upload a 70 Mb file via the web site. The length of time needed to transmit a 70 Mb file suggests that a high speed connection to the Internet is required to upload files the size of the ones containing the 3-D images. If data were to be transmitted via the Internet, sites would need to have T1 or greater access.

We established an FTP (file transfer protocol) site to test another method of transmitting large files from the sites to the Central Facility. We have not completed our testing but have gathered some information about the use of FTP.

- FTP can be run over SSL (secure socket layer), meaning that the transmission is encrypted and therefore secure.

- Software may be required to run on the sites' workstation or workstation provided by the study to support the FTP. If the workstation is configured to use FTP, the user will be more likely to easily transmit files to the Central Facility.
- A web site can link to an FTP site after a user passes their credentials to the FTP server. This needs to be tested to determine whether this will work if SSL is used.
- The FTP site can be configured so files can be dropped off and picked up or can only be dropped off.
- If software is needed, the costs of licensing the software will need to be investigated.

High-speed transmissions to the Internet are available from many sources as shown in **Table 1**. DSL and cable modem offer high-speed connections to the Internet but are primarily for use by home users and small businesses. Dedicated T1s and T3s (point-to-point connections) are secure. However, approximately $15,000 of equipment is required and the monthly cost based on the distance between the two points can be quite high. T1s and T3s to a local Internet provider (point-to-minipoint) are not as secure, but the monthly cost is reasonable. Internet2 is an emerging technology, but is not readily available. If we find a protocol, such as FTP, that will allow transmission of large files over the Internet, we can pursue these options further.

Based on the research we have done, we feel that for the pilot study transmitting data on CD/DVDs is the most secure, reliable, and cost-effective and the least burdensome method of transmitting the data. We suggest continuing research into FTP and other methods of data transmission that may emerge.

Using this approach, sonographers will enter the 2-D measurements, 3-D organ volume measurements, and other information on hardcopy forms and save the 3-D volume datasets ("raw" data) on a CD/DVD. The forms and CD/DVD will be mailed to the Central Facility by overnight courier. An advantage of transferring data this way is that sonographers can complete the study tasks for a patient without needing to go to another location where Internet access is available.

5.0 Summary

In summary, several methods have been considered for transmitting the 3-D volume datasets and the work completed to date indicates that the methods of transmission are limited. There is a potential option (file transfer protocol) that will need to be explored further that may allow the files to be transmitted, stored, and retrieved electronically. This document and the study protocols are based on a transmission method of CD/DVDs but all can be updated as new information dictates.

Remaining Questions:

- How much training is needed to ensure that the sonographer can obtain high quality 3-D volumes and determine organ volume measurements from these volumes of data?
- What is necessary to determine the most reliable and valid method for determining organ volume measurements?
- Are organs large enough in the first trimester to be able to determine organ volume measurements?
- If the Philips IU22 is to be used, a comparison of organ volume measurements obtained from this machine and the GE Voluson 730 would be useful.

TABLE 1

Summary of Data Transmission Methods Considered for the 3-D Ultrasound Feasibility Study

Method of Transfer	Description	Installation Time	Equipment Needed	Contract Period	Speed	Pros	Cons
CD (compact disk)	An optical digital audio disc that has a storage capacity of 650MB.	None	CDs	n/a	n/a	CDs are readily available. Secure.	Takes 24-48 hours to transfer the data from the medical facility to the central facility via an overnight carrier.
DVD (digital video disk)	A DVD-ROM is like a large CD-ROM that holds data and interactive audio and video material. The capacity of a DVD is 4+ Gb.	None	DVDs	n/a	n/a	DVDs are readily available. Secure.	Takes 24-48 hours to transfer the data from the medical facility to the central facility via an overnight carrier.
DSL (digital subscriber line)	A technology that dramatically increases the digital capacity of ordinary telephone lines (the local loops) into the home or office.	30 days	An Ethernet card and a telco supplied modem.		Tied to the distance between the customer and the telco central office. 0.5 Mb - 3 Mb.	Dedicated line. Secure.	Primarily for home users and small businesses. Must be available and supportable at the location.
Cable Modem	A modem used to connect a computer to a cable TV service that provides Internet access. Can dramatically increase the bandwidth between the user's computer and the Internet service provider, especially in the downlink (from ISP to user). Cable modems connect to the computer via an Ethernet port, which is an always-on connection. Ethernet is a shared medium, and the individual user's speed varies depending on number of simultanous users sending or receiving data on that cable segment.	30 days	An Ethernet card and a telco supplied modem.		4.0 Mbs for downloads; slower for uploads.		Primarily for home users and small businesses. Must be available and supportable at the location. Shared line
FTP (file transfer protocol)	A *protocol* used to transfer files over a TCP/IP network (Internet, Unix, etc).	n/a	n/a	n/a	Depends on the speed of the connection to the Internet.	Secure with software that supports SSL. Reliable.	Not secure. Must purchase software that supports SSL.
Dedicated T1 (point-to-point)	A 1.544 Mbps point-to-point dedicated, digital circuit provided by the telephone companies. T1 lines are widely used for private networks as well as interconnections between an organization's PBX or LAN and the telco.	45-60 days if the telco has service at both ends.	Router at originating point ~$2,000;~$10,000 for equipment at terminating point.	1 year	1.5 Mbs	Secure. Fast.	The monthly cost is typically based on distance. Distances of 250 - 500 miles may cost $2,000 - $3,000 per month. Equipment must be purchased for use at both points.
Dedicated T3 (point-to-point)	A 44.736 Mbps point-to-point dedicated line provided by the telephone companies. A T3 line provides 672 64-Kbps voice or data channels. T3 channels are widely used on the Internet.	45-60 days if the telco has service at both ends.	Router at originating point ~$2,000;~$10,000 for equipment at terminating point.	1 year	4.5 Mbs	Secure. Fast.	Monthly cost is typically based on distance. Distances of 700 - 1,000 miles may cost up to $100,000 per month. Equipment must be purchased for use at both points.

Method of Transfer	Description	Installation Time	Equipment Needed	Contract Period	Speed	Pros	Cons
T1 (point-to-minipoint)	Connection between a facility and a local Internet provider. The monthly cost is $300-$500.				1.5 Mbs	Secure with software that supports SSL. Fast.	
Internet2	The second generation of the Internet, developed by a consortium of >200 universities, private companies & U.S. government. Not developed for commercial use or to replace the Internet, but is the reincarnation of it, currently intended primarily for research. Whereas the Internet was first designed to exchange text, Internet2 is designed for full-motion video and 3-D animations.				600 Mbs	Secure.	Not widely available. Organizations may require major upgrades to their networks to connect to Internet2. Hops may be Internet rather than I2; this reduces the overall transmission speed to Internet speeds.