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PLATO'S CAVE — KNOWLEDGE-BASED MEDICINE OR BLACK SWAN TECHNOLOGY?

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Overview

Plato's CAVE™ is a presurgical planning, multidimensional "life space situation room" designed, developed, and introduced to clinical practice by the Department of Radiation Oncology at The Methodist Hospital, located in Houston's Texas Medical Center. At approximately 500 square feet, Plato's CAVE was specifically designed to permit a team of physicians to review all available diagnostic images of the patient (Figures 1a, 1b). The initial clinical focus was for interventions within the domain of surgical oncology, including radiation therapy, reconstructive surgery, and organ transplantation. This advanced clinical visualization process, supported by a novel and creative assemblage of FDA-approved, commercially available diagnostic imaging components, is available for all relevant patient care services within The Methodist Hospital System.

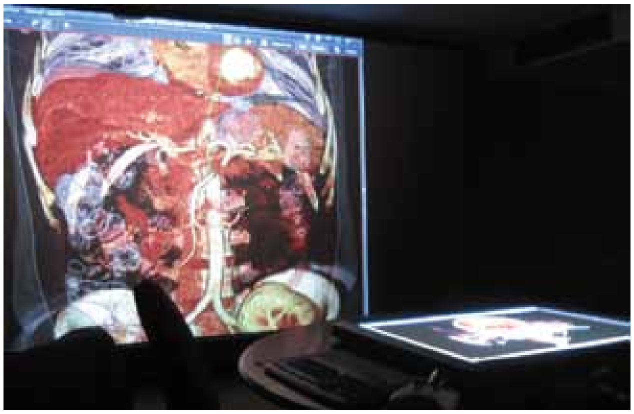

Figure 1a. Inside Plato's CAVE with large screen and virtual surgical table visualized with TeraRecon, Inc.

Figure 1b. Inside Plato's CAVE with large screen and laptop integrated visualization by BodyViz, Inc.

The underlying concept is that of a military flight simulator. As opposed to a commercial flight simulator, a fighter pilot environment is a multi-body simulation that records all of the plane's internal instruments and the pilot's actions with the digital fly-by-wire avionics system; its external position in relation to its global position; and, with GPS, the absolute spatial (X, Y, Z) position of the squadron and the aggressor(s) within its three-dimensional sphere of influence. This well-vetted process of recording input/output variables and resultant differences along the flight path of interaction is critical for pilots to learn from each other's experience what works well and what should be improved, all within a real-time frame of reference for action and reaction. The knowledge gained is now being used by unmanned aerial vehicles that are remotely piloted, not unlike the da Vinci surgical robot.

Figure 2. "The Visible Human" from the1995 National Library of Medicine, rendered with Fovia, Inc.

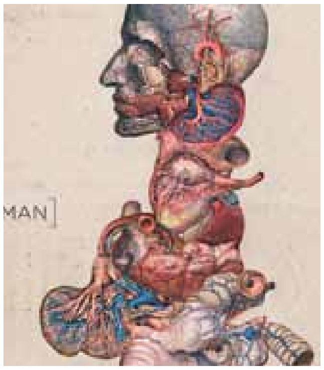

Figure 3. Archimedes Circulatory System from 287 B.C.

Plato's CAVE: Conceptual Beginnings

I first designed the single-user surgeon computer-augmented virtual environment (CAVE) concept in 2006 as the sole proprietor of a 20 ft x 15 ft glass-walled kiosk that was to be installed within one of The Methodist Hospital System's professional buildings. Initially called the Surgeons EDGE™, it was designed for cardiovascular surgeons who did not have the time or tools necessary to manipulate and integrate a series of patient-specific CT angiography (CTA) studies into an interactive 3-D volume that could be used to measure aortic grafts for individual patients. With the encouragement of Drs. Richard Geis, Samuel Henly, and Alan Lumsden, I designed a kiosk near the OR where cardiovascular physicians could fit aortic grafts to their patients on a 24/7 basis. The kiosk was to be fitted with a state-of-the-art 3-D TeraRecon large-screen workstation, and my role evolved into an "aorta tailor" who works with the physicians and sets up the procedure for measurement and validation.

In 2007, Drs. E. Brian Butler and Alan Lumsden were collaborating with IBM on a research project called the "Virtual Patient." They were attempting to use the National Library of Medicine's MRI-based Visible Human Project® as a base map for a detailed, image-guided, auto-segmented atlas of patient-specific CTAs (Figures 2 and 3). The Visible Human Project involved the creation of complete, detailed, 3-D representations of the male and female human bodies using CT and MRI slices.

Lumsden and Butler built on this concept with the acquisition of transverse CT, MR, and cryosection images of representative male and female cadavers. The male was sectioned at one-millimeter intervals, the female at one-third of a millimeter intervals; this level of resolution still exceeds the standard of care today. The Virtual Patient data set, with its detailed cross-sectional pathology photographs, was coregistered with medical imaging data sets of the body. The 3-D reconstructed virtual cardiovascular images were then automatically labeled and subsequently tagged with SQUID (superconducting quantum interference device) detectable anatomical markers for the proposed intra-operative image-guided system.

This process was designed to assist Drs. Lumsden and Butler in creating a vascular roadmap for the targeted delivery of a gene therapy "package" that could be activated with a time-release viral agent designed by Dr. Butler. Before it could be concluded, it was put on hold for two reasons: Dr. Butler was named chairman of the newly formed Department of Radiation Oncology at The Methodist Hospital, and Dr. Lumsden was named chair of Methodist's Department of Cardiovascular Surgery. In order to keep the project moving, both doctors asked me to work full-time with Dr. Butler at The Methodist Hospital and to look outside the box for nonclinical engineering solutions to the image-guided delivery system based on my previous scientific visualization experience.

I have worked for many years providing the visual system hardware and software for real-time fighter pilot training, 3-D seismic/geologic oil exploration, and pharmaceutical drug design using supercomputing tightly coupled to high-performance 3-D workstations. Previously, I had worked with Dr. Lumsden at Baylor College of Medicine on a peripheral arterial disease (PAD) multi-institutional clinical trial using 3T MRI with specialized bilateral coils for measuring plaque within the superficial femoral artery. Dr. Lumsden would repeat the phrase "it's all about the imaging" like a mantra for the vascular residents and fellows. Dr. Butler's vision for an interactive, real-time, 3-D radiation dose cloud for intensity modulated radiation therapy (IMRT) treatment planning was a logical and parallel extension of Dr. Lumsden's vision.

However, Dr. Butler needed to have a full integration of diagnostic imaging capabilities that would allow for clearer visualization and provide a more accurate, interactive tumor targeting and delineation system that could protect normal tissue from adverse radiation exposure. It was at this point that I decided to design an FDA-approved clinical diagnostic imaging integration that would be clinically relevant and make a difference in patient care.

Why "Plato's CAVE?"

When I asked Dr. Butler to think about a name for this pilot clinical project, he responded with "Plato's CAVE" from Book VII of Plato's *The Republic*, "The Allegory of the Cave," in which the prisoners see and

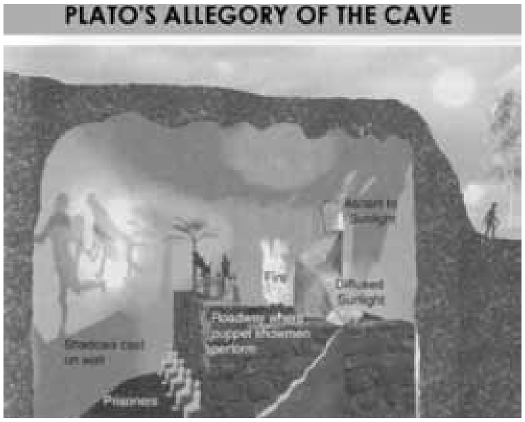

Figure 4. Plato, in *The Republic*, Book VII, 514a-520a.[1]

Figure 5. "The Anatomy Lecture of Dr. Nicolaes Tulp" by Rembrandt, 1632.

hear shadows and echoes cast by objects that they cannot see clearly (Figure 4 and 5).[1]

It was the perfect code name for exploring the art and science of "seeing" the invisible.

Dr. Butler's research over the past decade has been focused on image-guided radiation and gene therapies for cancer. In the past year, he and I have broadened the focus to include visualization-guided clinical interventions that are within the domain of surgical oncology, including reconstructive surgery and transplantation. This expanded focus was made possible by the development of an N-dimensional (space, time, color, and multimodality images) image-guided intervention system, more correctly a visualization system, that has been operational in our laboratory since April 2009.

Plato's CAVE: The Advanced Clinical Visualization Process

The current standard of care for medical imaging is to interpret slices of 2-D shades-of-gray images in an attempt to translate them into a physician's "personal virtual 3-D anatomical and disease world," then interpreting the problem and rendering a written diagnosis — granted, an expert professional diagnosis by a well-trained imaging specialist, but still an interpretation of a 2-D dataset nonetheless. Plato's CAVE raises the bar with an advanced clinical visualization process that creates 3-D images derived from a patient's DICOM image studies that have been pulled from Methodist's Picture Archiving and Communication System (PACS), from other institutional PACS via electronic transfer, or from CDs that patients bring with them. Regardless of the image source, the 3-D visualizations are ready for projection and viewing on a variety of screen formats within minutes. The region of interest is measurable, can be manipulated in three dimensions, and can be presented stereoscopically like the movie *Avatar.* This approach makes full use of the strengths of each imaging modality by displaying and/or fusing all of the images available for the patient (CT, MRI, PET and, soon, HR ultrasound) in a sequence of the events that are relevant to the treatment team. The scene is adaptable to all surgical interventions, from reconstruction through transplantation, and capable of bringing quality improvements to the diagnosis and treatment planning for many medical conditions.

Our technology is totally complementary to all standard-of-care imaging modalities currently in use and some that are in development, i.e., physiodynamic processes, beating heart, mitral valves opening and closing. There is a high level of clinical imaging and medical device industry interest in experimenting with or enhancing Plato's CAVE with natural user interactions. Our surgeons have discovered, once they work with this system, that they cannot easily justify returning to the current standard of viewing images for their patients. We have designed and integrated the CAVE to function as a node/portal on a physician grid or network. It is not an island: the visualization can be distributed to the scientist's or clinician's desktop because it is server-based, thin-client enabled, and HIPAA compliant.

The system offers enormous opportunity for educating primary care and referring physicians, patients and their families, medical students, residents and staff surgeons by narrowing the degree of uncertainty that each brings to the interaction (Figure 6 and 7). It also gives the medical team the ability to make a more informed decision regarding the best intervention or treatment of the disease. In some cases, the visualization has revealed previously unrecognized ancillary anatomical findings or additional disease complications.

Development, testing, validation and translation of this technology into practice will shape the metrics

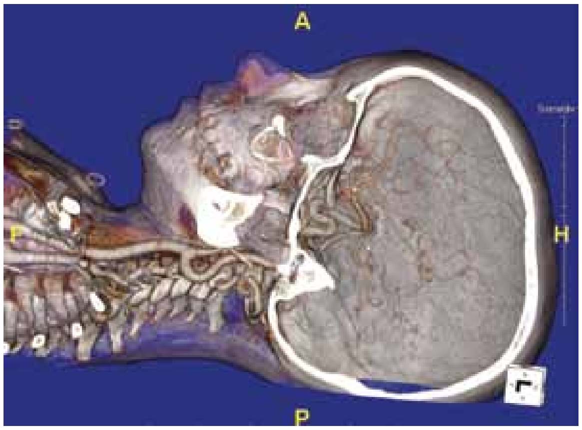

Figure 6. Virtual surgical table inside Plato's CAVE using TeraRecon, Inc. visualization

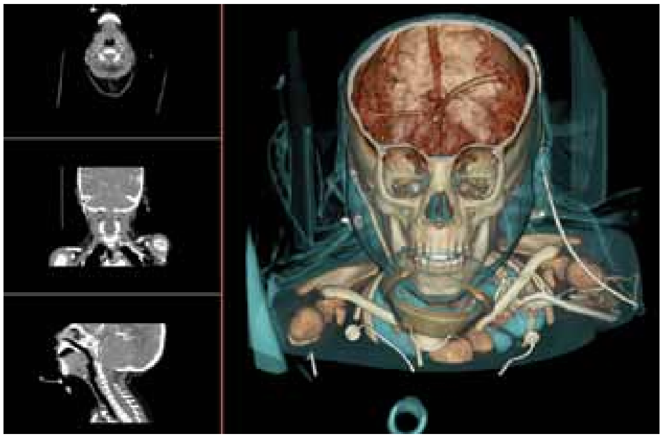

Figure 7. Virtual surgical table inside Plato's CAVE using TeraRecon, Inc. visualization.

necessary for adoption, and we anticipate that more refined tools will be developed to interact with the visualized patient. Ultimately, the images that are fused to create the visualized patient will be registered and superimposed to the real patient, and the instruments will interact with the patient to provide clinical interventions of the highest quality and safety. At the fundamental level, this system has universal applicability across all medical specialties and subspecialties and will allow the patient and physician to understand disease processes in ways never before possible.

We plan systematic evaluations of organ systems and their related disease processes. The hepatobiliary system provides a good example of the importance of doing this with high-fidelity visual data. Measuring the volume of this difficult-to-image organ is key to clinical decisions with respect to cancer diagnosis and therapy, among other medical conditions. Yet even simple volumetric evaluation represents a paradigm shift in the way that cancers are staged. For example, conventional staging of liver cancer is based on two dimensions — X and Y. Typically "size," as measured on axial CT or MRI images, is a major consideration, e.g., a 5 cm lesion will be classified as stage T2. In contrast, volumetric evaluation introduces a third dimension, Z, and may change the staging in significant ways. We now evaluate all hepatobiliary tumors volumetrically and within the last few weeks have begun mapping the arterial and venous branches so that surgeons can clearly avoid them while performing a resection.

Physician Response to Plato's CAVE

Plato's CAVE has generated a great deal of interest in and respect for its current ability and potential capabilities among our surgical colleagues. Some have used it multiple times to perform pre-surgery evaluation and planning, even to the extent of revising initial treatment plans or not doing an intervention based on the

Figure 8a. Virtual surgical table inside Plato's CAVE standard-of-care alongside interactive volume visualization.

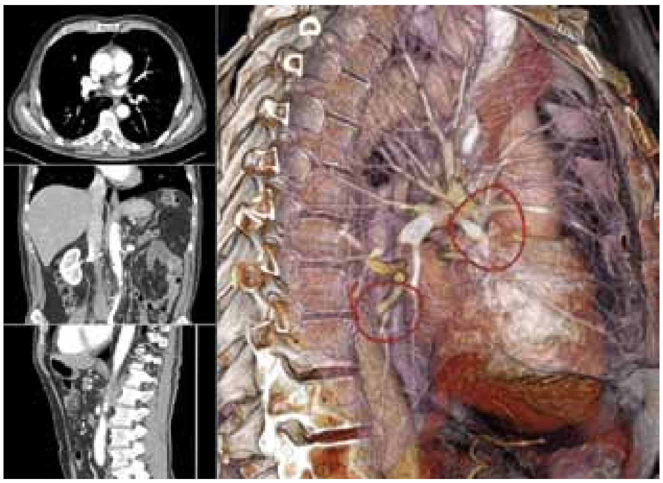

Figure 8b. Volume visualization with red finger tracings on virtual surgical table.

Figure 9. The Artery of Adamkiewicz identified by Dr. Sam Henly. Magnified virtual surgical table view inside Plato's CAVE using Siemens flash CT scan study with TeraRecon, Inc. visualization.

Figure 10. The Artery of Adamkiewicz, identified by Dr. Sam Henly, on the virtual surgical table inside Plato's CAVE using Siemens flash CTA scan with TeraRecon, Inc. visualization.

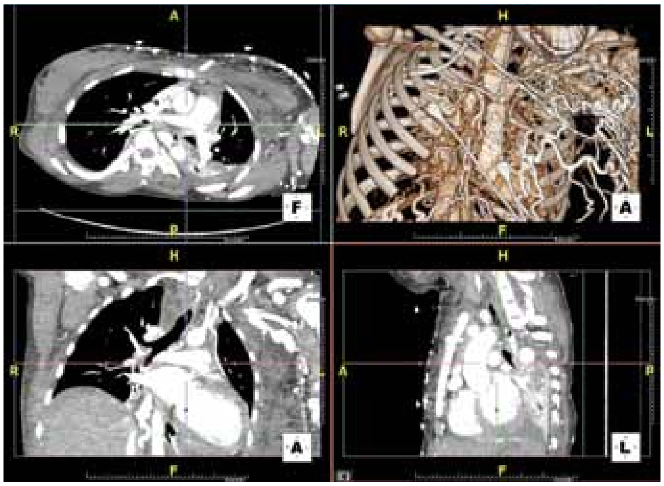

Figure 11. TeraRecon, Inc. visualization for planning the repair of esophageal varices that was more complicated than anticipated.

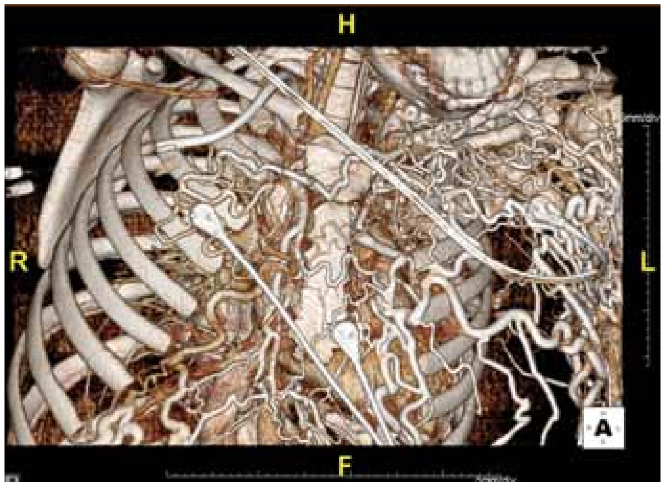

Figure 12. Virtual surgical table view inside Plato's CAVE using GE CTA scan study with TeraRecon, Inc. visualization for planning repair of esophageal varices.

additional information they gained from the 3-D visualization (Figures 8a and 8b).

Some surgeons have used our visualization as an education tool for their patients (Figures 9 and 10). The surgeons are impressed with the quality of the visualization, the ease and speed with which positions of the images can be changed, the ability to strip away tissue that blocks the view of the subject tissue, the fact that no contrast agents are required to achieve the visualization, the saving of time, and the unexpected ancillary findings (Figures 11 and 12).

On the other hand, some surgeons have said they do not see the need for such an environment because their experience overrides the real-time process and 3-D visualization that we provide, and that conventional imaging meets their needs. Yet, these same surgeons admit that the CAVE would have great value for medical education because of its clarity and responsiveness for accurately viewing patient-specific images and associated disease.

Clearly, N-dimensional visualization challenges current clinical practice paradigms. Unlike many technological advances in science and medicine, the constraint on acceptance and adoption of Plato's CAVE does not appear to be clinician resistance to change but rather the hospital's need for 1) metrics that will satisfy institutional risk assessment requirements, and 2) an effective process for disseminating the innovation along with best practice standards and protocols that are accepted by the general clinical staff. We routinely ask surgeons, "When you review currently available CT or MR studies for pre-surgical planning, have the standard diagnostic imaging and viewing tools provided you with the confidence that your treatment plan

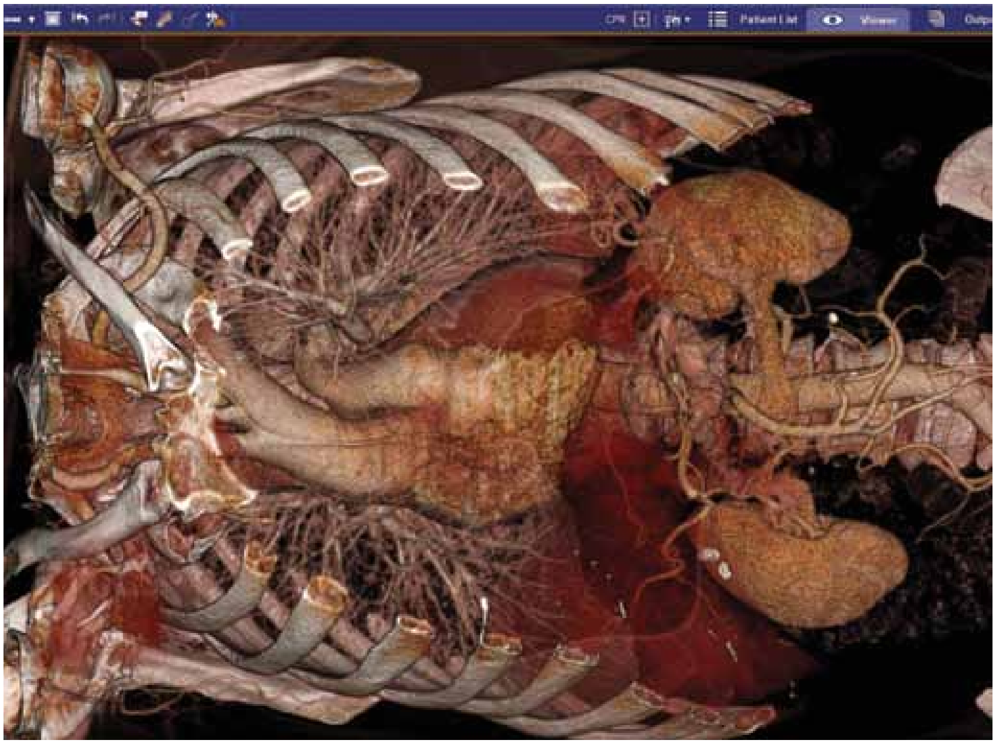

Figure 13. Looking down on the 36 in x 42 in multi-user virtual surgical table in Plato's CAVE using Siemens flash low-dose CT scan patient data with TeraRecon, Inc.

is based on objective visual anatomical accuracy versus subjective image estimation?" Their response is invariably "No."

In my 30 years within the scientific visualization world, I believe the experience that Plato's CAVE provides is approaching what some would call a black swan. The term "black swan" was a Latin term; its oldest reference is in the poet Juvenal's expression that "a good person is as rare as a black swan" ("*rara avis in terris nigroque simillima cygno*").[2] It was a common expression in 16th-century that derived from the old-world presumption that all swans must be white because all historical records of swans reported that they had white feathers. After the 1697 discovery of black swans in Western Australia,[3] the term metamorphosed to connote that a supposed impossibility may later be found to exist. Writer Michael Mandel used the term succinctly in an online issue of *Bloomberg Businessweek*: "The world is consistently capable of generating 'black swans' — outlier events, which have an extreme impact and retrospective (though not prospective) predictability."[4]

For the last few months, the clinical focus of the CAVE has evolved from physician-to-physician collaboration to physician-to-patient consultation and consensus. Almost 200 patients have been reviewed in the CAVE, and a word-of-mouth, patient-driven referral process has evolved because the involved physicians say that Dr. Butler's vision is providing an additional level of confidence, trust and understanding in what the physician and medical team can provide for each patient.

The Future of Plato's CAVE

We have begun to develop, adapt and test dual-reality tools (physical devices synched with a virtual clone of the device) that enable operator interaction with the patient-specific volume. Modeled to reflect the way surgeons use the real device, these tools will allow measurement and quantification of disease processes within the visualized patient (e.g., volume of a liver or blood vessel, size and location of an obstruction within the bile duct, how a pancreatic carcinoma encases the superior mesenteric artery, etc.). The physician can interact with the visualization of the patient before performing a procedure and record a scenario that can act as a look-ahead avoidance system, something the current da Vinci robots do not permit (Figure 13). This interaction will occur in numerous ways, one of which involves using a flat-panel, multi-user, multi-touch "surgical table" that allows multiple users to interact simultaneously with the visualized patient in a 1:1 mapped relationship. We are currently refining techniques for capturing a surgeon' s eye-hand movements in the OR that will enable us to build feedback loops based on

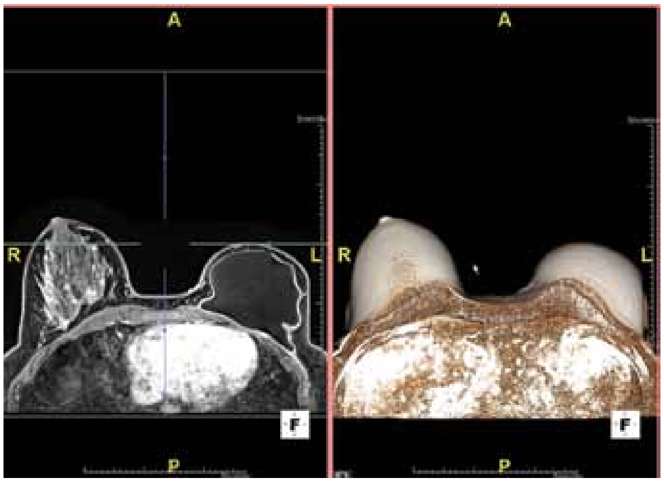

Figure 14. Reconstructed left breast with implant failure and disease in right breast; CT from Siemens.

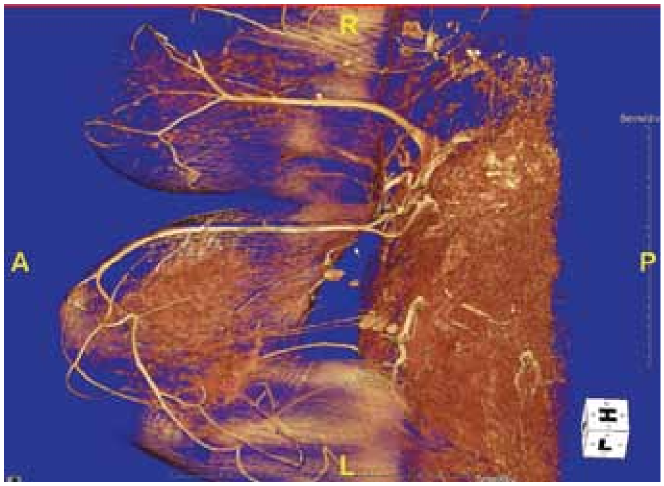

Figure 15. Toshiba breast MRI images without contrast, volume visualization on virtual surgical table. Please note clarity of IMAs.

Figure 16. Virtual surgical table, large screen and iPad.

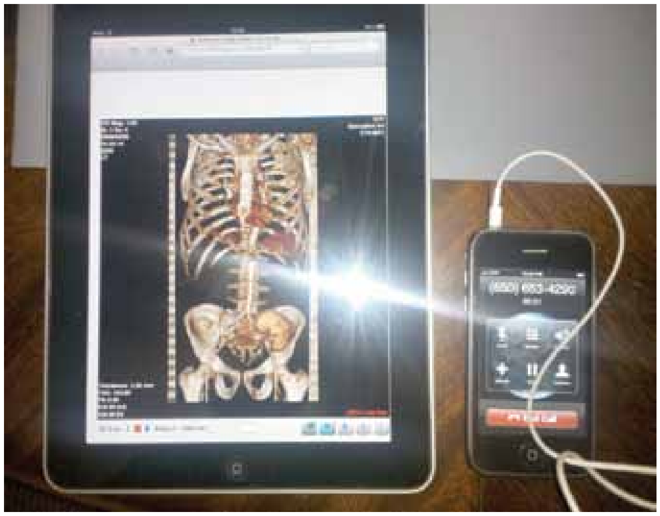

Figure 17. iPad and iPhone with transplanted kidney running remotely from area code (650).

haptic, hand-gesture, voice, and eye-tracking interaction between the operator and the patient visualization synchronously as it appears on the surgical table.

The CAVE's multi-dimensional interactive field of view includes the three spatial dimensions as well as motion, coordinated contrasting colors for different tissue types (such as muscle, organ, bone, nerve, blood vessels and ducts), time, and scale — in effect, it provides a virtual biopsy of any part of the visualized patient. Our first research and development project will soon enable Plato's CAVE to integrate and visualize physiological and biochemical parameters at the cell and molecular levels for breast cancer pattern finding and refined surgical reconstruction (Figures 14 and 15). Plato's CAVE will be tailored for an array of clinical practices, ranging from tumor board and surgical review processes within a hospital or department to surgeons' workstations linked to a high-performance computing cloud for new device development.

If Plato's CAVE is enabled to provide full support for physicians within The Methodist Hospital System, with the goal of using advanced clinical visualization techniques that integrate results of the patient's EMR with global bioinformatic markers, then the secondary goal of using CAVE software techniques that reflect time-saving workflow templates for individual physicians will provide an enterprise system that offers increasing levels of interactivity, speed and accuracy. It will also provide many opportunities, with our worldwide partners, to explore international clinical practice, translational research, and medical education with greater specificity for local environments.

We are currently using devices such as the iPhone and iPad with our surgeons and hope to include all physicians and medical students in a gradual, systematic, open-source process of sharing anatomic atlases and summaries of current specialized imaging protocols wherever they may be (Figure 16 and 17). Dual-reality visualizing (DRV) of patients can become a part of this open-source knowledge base as Plato's CAVE technology is developed, clinically vetted, released and able to record a visual record of surgical procedures.

Lessons being learned in Plato's CAVE are validating the clinical practicality of blending imaging, visualization and simulation with a CAVE measurement system that, with a dual-reality instrument or probe, offers six degrees of freedom within the virtual patient. What started with Dr. Lumsden's and Dr. Butler's mandate to "give me all of the imaging" is evolving into "calibrate, measure and record everything within a surgeon-specified 360-degree field of view" and providing a more accurate, patient-specific, pre-surgical planning and visualization-guided surveillance system (Figures 18a and 18b).

Conclusion

Plato's CAVE was built in 90 days and operational on April 1, 2009. Every day, it is refining an advanced clinical visualization acquisition process for viewing patient-specific, standard-of-care images within a multi-dimensional computer-augmented virtual environment. Its FDA-cleared technology is enhancing image acquisition protocols, diagnostic accuracy, treatment planning, post-treatment evaluation and follow-up while increasing patient safety and education, improving clinical productivity, and reducing costs.

Dr. Butler's vision of multiple physicians collaborating in a dedicated space and viewing all of the relevant diagnostic images on a large screen has been realized. Plato's CAVE has made and will continue to make a quality difference in patient care at The Methodist Hospital and soon will be deployed as a pre-surgical planning clinical imperative. As one young surgeon said, "It is the difference between knowing and guessing."

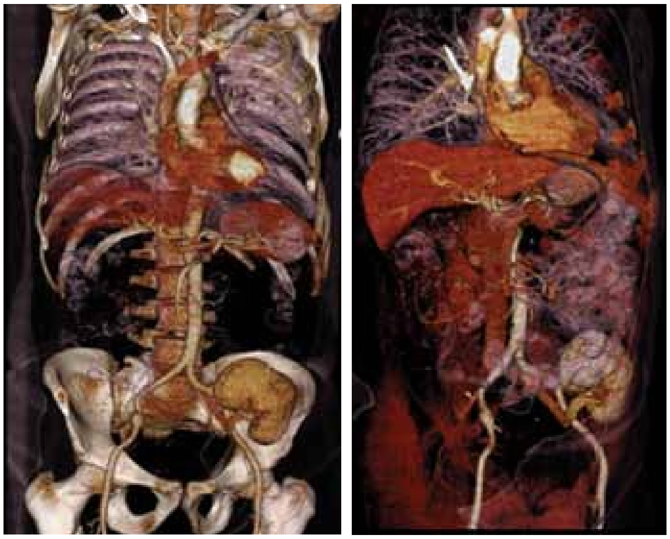

Figure 18a and b. Real-time 3-D virtual surgical table inside Plato's CAVE; patient study courtesy of OSIRIX with TeraRecon, Inc. reconstruction and 3-D visualization.

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