RESEARCH STRATEGY

1. Executive Summary of Predicate SBIR/STTR Phase I Grant and Team

The overall objective of our predicate STTR Phase I grant that started in June 2014 is to fully develop and conduct clinical translation of a novel technology that provides minimally invasive surgeons an ability to visualize exposed organ surfaces as well as structures hidden by them, together with a true appreciation of depth. A long-standing need in minimally invasive laparoscopic surgery has been to see *inside* and *around* a structure before dissecting, a need that currently used laparoscopes, even when high-definition and stereoscopic, cannot meet.

We achieve our objective by integrating 2 real-time surgical imaging modalities: (1) newly emerged 3-dimensional (3D) laparoscopic camera technology that allows visualizing the surgical anatomy with the highest image quality currently available and perception of true depth, and (2) laparoscopic ultrasound capable of visualizing hidden structures. We call the resulting visualization capability *stereoscopic augmented reality (AR)*, in which 3D laparoscopic video (the reality) is augmented with ultrasound findings, especially the blood vessels, ducts and tumors (see Figure 1).

Figure 1 Real-time overlay of ultrasound image on laparoscopic video creates the novel augmented reality visualization.

Children's National Medical Center and IGI Technologies are combining their complementary expertise to meet the goals of this project. Children's National, the site of the original research and development, brings unparalleled clinical image-guided surgery expertise and resources to facilitate clinical translation. IGI Technologies, a medical imaging small business, focuses on converting academic research into products.

Overall, the specific aims of the proposed research are to:
(1) create a compact, high-performance, operating room-ready 3D AR visualization system, and
(2) test, demonstrate, and characterize the 3D AR visualization system.

Our proposed I-Corps team will include the following three members.

Member Name	Role
William Plishker, PhD	C-Level Corporate Officer (CEO)
Mark Chandler, MBA	Industry Expert
Raj Shekhar, PhD	PD/PI

All three members are committed to the time requirements of the program.

2. I-Corps Team and Project Plan

The aims of our predicate STTR Phase I are designed to develop a compact, clinically viable system and test 2 milestones relating to acceptable image overlay accuracy and system responsiveness. Meeting these milestones will signal successful completion of Phase I and our readiness to transition to Phase II, which will include animal and human testing of the developed system.

The proposed system is novel in that no clinical system that combines 3D laparoscopic video and ultrasound exits. Successful execution of the proposed research will create a smart surgical visualization system that promises to provide surgeons greater confidence, minimize complications, shorten procedure times, reduce blood loss, and help expand the utilization of minimally invasive surgeries to beyond their 9%—12% current share of all surgeries. The anticipated benefits will apply equally to pediatric and adult surgery.
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Not only does this team meet the three core role requirements of the I-Corps program, the current and prior experiences of each team member demonstrate a deep commitment to technology transfer, commercialization, and entrepreneurship. The team has already been collaborating on developing a commercialization plan for the 3D AR technology, the focus of the funded STTR grant, and is therefore best prepared to continue their current effort under the I-Corps program as well. A detailed biography of each member is presented elsewhere in this application; we highlight here their most relevant experiences and specific connections to the current STTR project.

Dr. Plishker has been the CEO of IGI Technologies, the grantee small business, ever since its founding in 2007. He specializes in building and leading startups, and converting academic research into real-world products. His past experiences include work at three different Silicon Valley startups as an engineer and a member of a marketing and sales team as a Mayfield Fellow.

Mr. Chandler is a seasoned business executive and a recognized expert in commercializing intellectual property (IP) and technology. He is the founder of Upstream Partners, a specialty advisory firm that helps its clients with their IP needs in all aspects of early-stage technology, product development, and business creation. Mr. Chandler has been involved in the creation or funding of more than 10 companies, all based around emerging technology and IP assets in areas such as medical technology, medical information, advanced electronics and photonics.

Dr. Shekhar is a serial innovator of medical and surgical imaging technologies and an entrepreneurial academic with 15 years of experience. Two of his prior inventions (intravascular ultrasound image analysis and cardiac CT) have led to successful commercial products. He is currently a principal investigator within the Sheikh Zayed Institute for Pediatric Surgical Innovation at Children's National. He is also the lead inventor of the underlying AR technology and the PI of the STTR Phase I grant.

Drs. Plishker and Shekhar, who together founded IGI Technologies, are collaborators on the STTR project and have been partnering on technology transfer and product development efforts for a number of years. Among his many roles, Mr. Chandler serves as a business consultant and entrepreneur-in-residence for the Sheikh Zayed Institute and advises institute PIs, including Dr. Shekhar, on technology commercialization. Mr. Chandler has been assisting Dr. Shekhar in defining a commercialization strategy for the 3D AR technology.

Since the start of the STTR Phase I grant project in June 2014, Dr. Plishker, Mr. Chandler and Dr. Shekhar have been engaging frequently in IP and commercialization strategy discussions pertaining to the 3D AR technology. Maintaining the same team for the I-Corps program will minimize any new member onboarding issues and, most important, will build on the existing working relationships, a thorough understanding of the technology and its current state of development, and shared vision for the technology.

This proposed team is also in a position to benefit maximally from the I-Corps program as it has already conducted background research into competitive IP landscape, value proposition, market assessment, reimbursement models, and identifying a preliminary commercialization pathway. With

new knowledge and information gained from the I-Corps program, the team is capable of and looks forward to a thorough vetting from potential customers and industry experts of these early concepts and refining, realigning and/or pivoting their initial plan to maximize commercialization success.

Over the last three years, the AR technology has been a major focus of Dr. Shekhar's research efforts. He has led development of the 3D AR technology from a concept to a working prototype currently being tested in the clinic. As expected, he is passionate about its full development into a finished product. Much of the success of IGI Technologies also depends on successful conversion of the work of this STTR project into a successful product. Dr. Plishker has therefore chosen to get involved in the I-Corps training personally and will make the time necessary for it. Guiding successful commercialization of the 3D AR technology, one of the flagship initiatives of the Sheikh Zayed Institute, is also priority of Mr. Chandler's. As an investor in early-stage technologies, Mr. Chandler sees the value in a structured validation of the 3D AR product through the I-Corps process and views the opportunity as a means to position the technology for private investing in the future. As is evident, each of the three members has personal as well as collective stake in successful commercialization and is committed to meeting the time requirement of the I-Corps program.

3. Potential Commercial Impact

Commercial potential

The current research originated at the Sheikh Zayed Institute for Pediatric Surgical Innovation, an institute established in 2010 with innovation as its founding philosophy. The Institute promotes innovation and views technology commercialization as the culmination of all research and development activities. Significant resources are available within the Institute and processes are in place to screen projects by their commercialization potential when they are first proposed and periodically throughout their conduct. Our project, too, has gone through the Institute's rigorous commercialization potential screening processes. At this point, we feel confident about the commercialization potential of our technology in large part due to the validation it has received to date.

One of the forums to assist with technology commercialization within the Institute is its Business Advisory Council. The Council is made of prominent business leaders, serial entrepreneurs, and technology transfer experts. Dr. Shekhar presented the 3D AR technology before this Council in May 2013 and again in May 2014. The overall feedback of the Council regarding the commercial potential of the technology has been enthusiastically positive. The Council appreciated the progress made in a year, thought that the potential market was larger than presented, and that the technology held the promise of near-term commercialization. The team has been incorporating the recommendations of the Council for readying the technology for commercialization success.

We are entering a large and fast growing market in medicine: image-guided minimally invasive surgery equipment. While other areas of medicine are experiencing lowering reimbursements and other downward cost pressures, the market for general and pelvic endoscopes will grow from $804 million in 2013 to above $1 billion in 2018 (MIS Trends 2014: Improving Visualization [1]). High-definition 3D, technologies to address loss of visibility, and fluorescence imaging are newer innovations in the market place that will drive growth in this space. This fits well with our own positioning in the market as our innovation incorporates high-definition 3D and competes favorably with fluorescence imaging in making normally hidden anatomy visible. We have estimated the US market for our technology to be in the $100-$150 million range. This assumes our technology being available in 5% of all ORs in the United States.

Target customer

Minimally invasive laparoscopic surgeons are the end users of our technology. In fact, the technology is being developed in close partnership with two minimally invasive surgeons at Children's National: Dr. Timothy Kane, a general and thoracic surgeon, and Dr. Craig Peters, a robotic urologic surgeon. Both are co-investigators in the STTR project. Dr. Kane is also leading the IRB-approved clinical evaluation of the existing prototype. With such a close clinical collaboration, our technology development has already been shaped by forward thinking end users. Our collaborating surgeons have also contributed to the development of the commercialization strategy and the proposed I-Corps team plans to continue to consult with them going forward.

While the minimally invasive surgeons are the end users, we believe, surgical imaging companies can be the providers of our technology and are also our customers. Our innovation can be viewed as an advanced imaging option that these companies could offer to the hospitals and surgeons through their existing sales and marketing channels. To this end, we have demonstrated our technology to BK Medical (one of the two leading surgical ultrasound vendors), Visionsense (an early-stage 3D endoscopy vendor) and Stryker (a leading endoscopy vendor). The feedback from each has been that our technology is an important "value add" and could be a "product differentiator" for them. We continue to discuss our technology with these companies with the goal of a potential strategic partnership. One of our specific plans for the I-Corps program is to conduct interviews with more such companies.

Clinical need and current alternatives

A fundamental limitation of conventional laparoscopic surgery is that internal anatomic structures, i.e., structures beneath the visible organ surfaces, are not visible to the operating surgeon. While the basic anatomy is known through preoperative imaging, this, by necessity, changes during the surgical procedure. Our innovation provides the surgeon the much-needed complete visualization of the surgical anatomy throughout the procedure. In any ablative or reconstructive surgery involving solid organs (liver, kidney, and pancreas, for example), the relationship of the organ parenchyma, vasculature, ductal structures, and the tumor must be fully appreciated for oncological and reconstructive success. With our technology, the surgeon can optimize tumor resection or abnormal tissue removal, while concurrently protecting normal tissues and limiting blood loss.

Incorporated in our innovation is also 3D vision, which replaces a relatively flat representation of the surgical anatomy with a representation with all depth cues. This feature, in essence, brings the surgical efficiency benefits of robotic surgery associated with 3D vision to conventional laparoscopic surgery.

Most minimally invasive surgeons currently address these unmet needs with a general knowledge of the anatomy from preoperative images and experience. Doing so is slow and tedious as well as high-risk. The risk lies with either excessive collateral damage to normal tissues or inadequate oncological resection risking tumor recurrence. The location and anatomic configuration of the pathological anatomy is generally highly variable and, to adequately protect the benign structures, a dynamic real-time knowledge of their relationship to the pathological anatomy with good depth perception, as provided by our technology, is essential.

For certain selected procedures, depending on the preoperative assessment of the complexity of the surgical anatomy, surgeons use other assistive technologies to visualize internal anatomic structures intra-operatively. In laparoscopic cholecystectomies (minimally invasive gall bladder removal surgeries), x-ray-based cholangiography is used. Limitations of cholangiography are radiation, lengthy setup time, and contrast administration. Moreover, it provides just a single snapshot of the anatomy, not a dynamic image. Laparoscopic ultrasound is also utilized in some cases; however, ultrasound images, when presented separately away from the visual information unlike in our innovation, pose interpretation challenges and are not as surgeon friendly. The task of mentally correlating the ultrasound information with the visual image is difficult and variable with surgeon expertise. Finally, fluorescence imaging is an emerging option for visualizing subsurface structures. Limitations of this technology are the need to administer ICG (a dye) and an imaging depth of only a couple of millimeters.

Competitive advantage

Our innovation addresses most limitations of the existing alternative solutions. First of all, our solution does not require any contrast or drug administration, making it easier to fit into the existing workflow. Second, the use of ultrasound in our solution does not impose any imaging depth limitations as with fluorescence imaging. Compared to standalone ultrasound, we enhance the usefulness of the information present in ultrasound imaging by integrating it with the visual image of the surgical anatomy. Furthermore, all of this is done on a real-time basis and can be repeated as often as clinically necessary and desired. The Doppler mode of ultrasound can also be optionally turned on to highlight the vasculature. Finally, compared to other methods our innovation has cost advantages.

Price estimate

Our current price estimate for the 3D AR product is $50K, and this estimate has figured in our math for market size estimation. This price point has been established considering a number of factors: material and production cost, cost of similar products, consultations with collaborating surgeons and a hospital administrator, hospitals' capital asset approval thresholds, and the ability of the hospital to amortize the investment. We are open to revisiting these and additional factors and possibly revising this price point based on interviews of a much larger pool of stakeholders of the technology.

4. Project Plan

We have a fully operational prototype as shown in Figure 2. This prototype has been tested in phantoms and animals and we have published these results [2, 3]. We have indeed taken care of protecting our IP and have a pending patent [4]. More recently, with IRB approval, we have begun testing the prototype clinically and have imaged the hepatobiliary anatomy successfully in three patients referred for laparoscopic cholecystectomy (see Figure 3). A movie clip showing the resulting AR visualization is available at https://www.youtube.com/watch?v=o2gRihiy-wc. This novel mode of visualization clearly shows the bile ducts and, in this particular example, a stone in the cystic duct in the surgical field of focus. It should be appreciated that these internal structures would not be visible during a conventional laparoscopic procedure.

Figure 2 Current 3D AR visualization prototype.

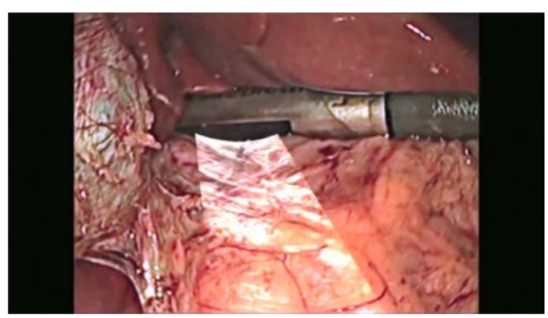

Figure 3 AR visualization of hepatobiliary anatomy during laparoscopic cholecystectomy.

This predicate STTR grant is motivated in a large part by our experience of using this prototype in the OR. This has included the feedback of Dr. Kane, our clinical lead, and other surgeons regarding the usability of the prototype and the team's experience in making the prototype work in a real-world setting. The clinical experience has led to many system improvement recommendations for making the technology clinically viable, robust, easy to use, and fit seamlessly within the existing workflow of the OR. Two major recommendations—switching from line-of-sight optical tracking to electromagnetic (EM) tracking and reducing the form factor of the prototype—are being addressed in the STTR project. We have already begun testing EM tracking and plan to present our initial results at a scientific forum in September 2014 [5]. Other technical developments are also being worked on.

At the end of Phase I, we will have completed our technical development and have a 2nd-generation prototype ready that incorporates EM tracking for spatial referencing of imaging devices in the OR and uses a laptop computer (as opposed to a bulky desktop) to run the 3D AR visualization software. The associated system testing will ensure that the system performance (accuracy and responsiveness) is maintained. The 2nd-generation system will be closer to a finished product and one that could be operated by the OR staff independently after training.

We plan to propose animal and clinical studies involving the 2nd-generation prototype in the Phase II grant application, but we believe a more advanced prototype developed with Phase I funding and with feedback from field testing will position the team well to seek sponsored research and/or industrial partnerships. First, a compact design will allow us to demonstrate the prototype at scientific conferences and trade shows. Second, it will allow potential acquirers to visualize that our technology could be integrated into their own larger imaging systems.

During the execution of the Phase I project, IGI Technologies will also conduct a professional marketability analysis and generate a list of potential licensees. It will then pursue both corporate and angel/venture financing avenues for product development, multi-center clinical trials, and seeking regulatory approvals.