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| Fiscal Year: | FY 2009 | Task Last Updated: | FY 08/12/2009 |
| PI Name: | Crum, Lawrence A. Ph.D. | | |
| Project Title: | Smart Therapeutic Ultrasound Device for Mission-Critical Medical Care | | |
| Division Name: | Human Research | | |
| Program/Discipline: | NSBRI | | |
| Program/Discipline--Element/Subdiscipline: | NSBRI--Smart Medical Systems and Technology Team | | |
| Joint Agency Name: | TechPort: | Yes | |
| Human Research Program Elements: | (1) ExMC :Exploration Medical Capabilities | | |
| Human Research Program Risks: | (1) Medical Conditions :Risk of Adverse Health Outcomes and Decrements in Performance Due to Medical Conditions that occur in Mission, as well as Long Term Health Outcomes Due to Mission Exposures | | |
| Space Biology Element: | None | | |
| Space Biology Cross-Element Discipline: | None | | |
| Space Biology Special Category: | None | | |
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| Zip Code: | 98105-6606 | Congressional District: | 7 |
| Comments: | | | |
| Project Type: | GROUND | Solicitation / Funding Source: | 2007 Crew Health NNJ07ZSA002N |
| Start Date: | 08/01/2008 | End Date: | 07/31/2012 |
| No. of Post Docs: | 3 | No. of PhD Degrees: | 1 |
| No. of PhD Candidates: | 2 | No. of Master' Degrees: | 0 |
| No. of Master's Candidates: | 0 | No. of Bachelor's Degrees: | 2 |
| No. of Bachelor's Candidates: | 2 | Monitoring Center: | NSBRI |
| Contact Monitor: | Contact Phone: | | |
| Contact Email: | | | |
| Flight Program: | | | |
| Flight Assignment: | | | |
| Key Personnel Changes/Previous PI: | | | |
| COI Name (Institution): | Bailey, Michael (University of Washington) Sapozhnikov, Oleg (University of Washington) Carter, Stephen (University of Washington) | | |
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| Performance Goal No.: | | | |
| Performance Goal Text: | | | |

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| | <p>The major goals of this effort is to utilize existing ultrasound platforms and the concept of image-guided therapy to control traumatic bleeding, ablate cancerous tumors, and diagnose and clear kidney stones. Our methods and devices are countermeasures to specific risks described in the Human Research Program Integrated Research Plan, viz.,</p> <ol style="list-style-type: none"> (1) Lack of advanced therapeutic capability, (2) lack of capability to treat renal stones, and (3) lack of non-invasive diagnostic imaging capabilities. <p>The original specific aims are:</p> <p>Specific Aim 1: Support ongoing leveraged efforts in Acoustic Hemostasis (AH) and HIFU Tumor Ablation (TA) by addressing fundamental scientific issues as well as to ensure NSBRI relevance.</p> <p>Specific Aim 2: Develop methods and technology that would enable detection of renal stones with ultrasound.</p> <p>Specific Aim 3: Develop technology and perform in vitro studies of stone comminution.</p> <p>Specific Aim 4: Utilizing technology and protocols developed in SAs 2 and 3, perform in vivo studies in a porcine model.</p> <p>(2) The key findings and associated research productivity for year 1 are:</p> <ul style="list-style-type: none"> - Developed an automated ultrasound guided high intensity focused ultrasound (HIFU) system to detect and stop bleeding: Published paper. - Began initial investigation of HIFU induced tumor specific immune response in collaboration with Fred Hutchinson Cancer Research Institute: Obtained NIH funding to support a Postdoctoral fellow on the work. - Developed a body of evidence on methods to accelerate HIFU therapy with the use of shock waves: Papers published. - Tested new Doppler ultrasound-based kidney stone detection method in vitro, in animals, and in humans: Filed 3 Records of Invention with the University of Washington TechTransfer Office. <p>Task Description:</p> <ul style="list-style-type: none"> - Developed method to use focused ultrasound to move kidney stones and stone fragments within the kidney to expedite stone clearance: Presented work to American Urology Association. - Miniaturized device to size stone fragments for safe extraction and tested operation in kidney: Submitted U.S. utility patent application and published paper. - Developed correlation between ultrasound-induced and monitored vasoconstriction; discovered that vasoconstriction reduces injury during stone fragmentation therapy: Published paper. - Participated in the generation of a white paper through gap analysis of medical risk 4.15 (Lack of lithotripsy or other capability to treat a renal stone) by the JSC Exploration Medical Capability element of the Human Research Program. - Copyrighted and licensed technology describing new HIFU sources and test equipment. <p>(3) These findings are self-explanatory, but we wish to highlight the broader impact on kidney stone disease. Our new detection technique requires only a software change, at most, to existing ultrasound technology on board ISS. It is sensitive and easy to use. Our belief is that this approach will provide NASA with the capability to detect even small, asymptomatic stones. The next phase of our work will be to use focused ultrasound (which could also be generated with only modest software reprogramming of the existing ISS ultrasound device) to dislodge the stone and push it toward the opening of the ureter where it could be naturally passed. In this way, a potential critical clinical problem would be solved by early diagnosis and prevention, rather than by last-minute and difficult therapy. This methodology has obvious and significant earthbound utility as well.</p> <p>(4) Our future plans will focus on continued automation, cancer treatment, and the prevention of complications from kidney stones. We have obtained access to a programmable ultrasound imager that we will program to test our new stone detection algorithms. The immune response study, initiated by seed funds from our NSBRI cost match, will be continued under NIH sponsorship; hopefully, it will be determined that HIFU can induce a systemic tumor-specific immune response in mice. Investigation and improvement of the stone detection technique will continue by direct comparison of simulation and measurement. The technique to detect stones at pre-symptomatic levels will be tested against standard ultrasound, fluoroscopy, and CT in patients. Acceleration of stone passage by focused ultrasound will be investigated in a porcine animal model.</p> |
| <p>Rationale for HRP Directed Research:</p> | <p>In general, this project advances a new technology- high intensity focused ultrasound (HIFU) toward clinical application. HIFU machines have treated over 100,000 cancer patients in China and over 5,000 in Europe and Japan. The only indication approved by the FDA for the use of HIFU on patients is that of uterine fibroids. Dozens of start-up companies and the big three ultrasound companies - GE, Philips, and Siemens - are developing HIFU machines. We are beginning to license our intellectual property to the commercial sector. We were intimately involved in the founding of the International Society for Therapeutic Ultrasound and currently play major roles in its administration. Similarly, we have helped establish the International Kidney Stone Institute and have authored consensus reports on lithotripsy and ultrasound safety.</p> <p>Specifically our work this year has provided the following Earthbound benefits, viz.,</p> <ol style="list-style-type: none"> 1. We demonstrated a way to automate the detection and treatment of bleeding. 2. We have designed and initiated a study to test the hypothesis that HIFU can generate a systemic immune response and have high hopes for progress in this area. 3. We have offered the HIFU community significant insight into how to plan, execute and monitor HIFU treatments. For earthbound HIFU, we have raised considerable concern over the accuracy of the gold standard (MR thermometry) used to "ensure" heating only where desired. <p>Research Impact/Earth Benefits:</p> |

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| | <p>4. Our efforts to develop a Doppler ultrasound-based, kidney stone detection method has several applications. It appears at least as good a fluoroscopy in targeting and could therefore replace this approach and its ionizing radiation. It also can be used real-time and therefore could compensate for respiratory motion during treatment. Lastly, an accurate ultrasound imaging system could be used in the urologist's office to localize stones and to replace the need for CT scans.</p> <p>5. Our new method to use focused ultrasound to move kidney stones could be used whenever residual stones are observed after treatment. These stones get trapped and do not pass naturally. They then serve as a nucleus for future stones.</p> <p>6. Our miniaturized device to size stone fragments may soon be used during ureteroscopy to determine stone size before attempting to extract stones too large to pass through a finite-sized lumen.</p> <p>7. We have licensed new HIFU sources and test equipment to a vendor who will provide these tools to researchers, clinicians, regulators, and manufacturers to accelerate the implementation of clinical HIFU applications.</p> |
| Task Progress: | <p>The second tier research tasks described in the proposal are listed below and the progress on them for this year is as follows.</p> <p>Task 1A1. Perform studies of bleeding detection in a flow-phantom model. A model and a method to excise but not detach the femoral arteries in live pigs have been developed.</p> <p>Task 1B1. Perform studies to determine pressure and temperature in ex vivo tissue exposed to HIFU. A paper co-authored by M.S. Canney, V. A. Khokhlova, O.V. Bessonova, M. R. Bailey, and L. A. Crum, entitled "Millisecond boiling produced by high intensity focused ultrasound," was submitted in February 2009 to the journal Ultrasound in Medicine and Biology.</p> <p>Task 2A. Develop new stone detection techniques based on radiation force and reverberation responsible for the twinkling artifact and vibroacoustography. We have completed considerable data collection and have begun an analysis of the data to improve understanding of the mechanisms and algorithms for use. Three records of invention describing the evidence for this new understanding have been filed. We also reported progress in the following paper: A. Shah, M. Paun, J. Kuciewicz, O. A. Sapozhnikov, M. Dighe, H. A. McKay, M. D. Sorensen, and M. R. Bailey, "Investigation of an ultrasound imaging technique to target kidney stones in lithotripsy," J. Acoust. Soc. Am., 125(4, Pt. 2), 2620 (2009).</p> <p>Task 2B. Investigate stone-sizing technology in tissue. We have submitted for publication our progress in this task in the following article: M.D. Sorensen, J.M.H. Teichman, and M.R. Bailey, "A Proof of Principle of a Prototype Ultrasound Technology to Size Stone Fragments During Ureteroscopy," J. Endourology in press 2009, We have also filed U.S. and international utility patent applications, and are negotiating licensing.</p> <p>Task 3A. Utilize the YUANDE HIFU tumor ablation device as a platform for determining the acoustic protocols necessary for ultrasound-based stone comminution. No significant progress to report. For business reasons, effort has shifted to a second clinical device.</p> <p>Task 3B. Engineer and optimize an image-guided, two-frequency HIFU system for renal stone comminution. In year one, we have focused on moving small stones within the kidney with ultrasound to facilitate natural stone clearance. Results were reported at the American Urology and Laparoendoscopic Surgeons meetings. Stone comminution work is scheduled to continue later in the Research Project.</p> <p>Task 4A. Perform in vivo tests of the imaging protocols developed in Task 2. Investigations are underway for stone detection not only in animals but in humans. Human protocols have been approved and added to the grant.</p> <p>Task 4B. Perform studies to determine the potential for HIFU-induced stone comminution as well as any associated tissue injury. In vivo studies of stone clearance are underway.</p> |
| Bibliography Type: | Description: (Last Updated: 03/22/2019) |
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| Awards | Bailey MR. "Re-elected AIUM Bio-effects committee, February 2009." Feb-2009 |
| Awards | Crum LA. "Invited tutorial lecture at 2009 IEEE Ultrasonics Symposium, September 2009." Sep-2009 |
| Awards | Khokhlova TD. "NIH T32 Training grant postdoctoral fellowship, July 2009." Jul-2009 |
| Awards | Bailey M. "Elected to the Governing Board of the International Society for Therapeutic Ultrasound, June 2009." Jun-2009 |
| Awards | Sapozhnikov OA. "Fellow of the Acoustical Society of America, June 2009." Jun-2009 |
| Dissertations and Theses | Canney MS. "Nonlinear enhancement of heating due to shock formation in high intensity focused ultrasound fields." Dissertation, University of Washington, June 2009. , Jun-2009 |
| Papers from Meeting Proceedings | Crum L, Bailey M, Canney M, Chen H, Matula T, Mc Innes C. "Direct observation of surface particle removal by an ultrasonic toothbrush." Acoustics '08 Paris, Joint meeting of the Acoustical Society of America, ASA, the European Acoustics Association, EAA, and the Société Française d'Acoustique, SFA, Paris, France, June 29-July 4, 2008. Proceedings of Acoustics '08 Paris, Joint meeting of the Acoustical Society of America, ASA, the European Acoustics Association, EAA, and the Société Française d'Acoustique, SFA, Paris, France, June 29-July 4, 2008. , Jul-2008 |
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| Patents | 111. Patent, June 2008. Jun-2008 Bailey MB, Carter S, Kaczowski P, Kucewicz J. "Method and system for automation of focused ultrasound treatment." |
| Patents | None yet. Patent in process, May 2008. May-2008 Bailey MB, Sorensen MD, Teichman J. "Method and device to measure stone size in surgical removal of kidney stones." |
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| Significant Media Coverage | Shah A, Paun M, Kucewicz J, Sapozhnikov OA, Dighe M, McKay HA, Sorensen MD, Bailey MR, Crum LA. "Lay version of paper for Meeting Press: Investigation of an ultrasound imaging technique to target kidney stones." Acoustical Society of America lay paper, May 2009. http://acoustics.org/pressroom/httpdocs/157th/bailey.html , May-2009 |