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Development of an X-Ray Catheter Final Report CRADA No. TC-1265-96

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Development of an X-Ray Catheter

Final Report
CRADA No. TC-1265-96

Date: 5/26/00 Revision: 3

A. Parties

The project was a relationship between the Lawrence Livermore National Laboratory (LLNL) and Interventional Innovations Corp. (IIC). IIC later became XRT Corp. (XRT). After this CRADA project was completed but before the Final Report was executed, XRT was acquired by Medtronic AVE ("Medtronic"). IIC, XRT, and Medtronic are collectively referred to as "Participant."

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B. Project Scope

The goal of this CRADA project was to develop a catheter-based x-ray source to provide treatment of restenosis in arteries with a radiation source which can be precisely controlled and turned on and off at will.

C. Technical Accomplishments

LLNL undertook the development of prototype x-ray catheters under a funds-in CRADA with IIC. The project was initiated in March 1996 and terminated in April 1997.

Initially multiple operating modes, geometries, and materials were evaluated prior to development of a prototype system. Anode-cathode geometries and materials were tested for electrical and x-ray performance in a test cell that was assembled for this purpose. A cathode for the baseline design was developed at Sandia and tested at LLNL. Supporting electric field calculations were conducted to assist in the design optimization.

The absolute x-ray spectrum was measured from a prototype geometry operating in the test facility. The measured spectrum was then used to calculate a delivered dose to blood vessel walls. An x-ray dose of 0.1 Gy/sec/100 microamps of current was calculated at a position 1 mm from the inner wall of the blood vessel.

Several cables to be used in prototype x-ray catheters were tested for high voltage operation and breakdown. Cables meeting the requirements for size, voltage, and current were determined.

Fabrication techniques were developed for producing a prototype x-ray emitter with high voltage cables connected. This included the development of brazing techniques for the materials used. An activation process for establishing the vacuum in the emitter and for initial conditioning of the electrodes was developed. A system for establishing the vacuum and for initial conditioning of the electrodes was developed and demonstrated.

Several x-ray emitters with a crimp-off configuration were fabricated, conditioned, connected to high voltage cables and operated independently of any vacuum support equipment. X-ray yield, voltage, and current were measured during operation. A unit configuration was demonstrated with a shelf life of 3 months. The maximum shelf life was never determined as the testing was stopped when the project was put on hold in April 1997.

Deficiencies in some of the materials used were determined through testing and characterization and recommendations for improved materials were made.

A method of stabilizing the operating current and voltage of the x-ray source was developed and demonstrated.

The thermal load produced by the x-ray catheter was assessed in both simulations and measurements. A simulated thermal load was produced using a laser heated catheter. This was inserted in instrumented blood vessels segments and the temperature at various locations was monitored as a function of blood flow and heat load. LLNL's results indicate that a catheter operating with an electrical power of 2.6 watts would not heat the blood vessel wall more than 5 degrees C above body temperature as long as blood flow was maintained at a minimal level, for some device and blood vessel sizes. A system that would allow x-ray catheters to be used in thermal measurements with blood vessels was developed.

D. Expected Economic Impact

The economic impact is expected to be substantial. LLNL believes the x-ray catheter will be used to treat arterial restenosis. This disease affects approximately 250,000 patients in the US and about 400,000 worldwide. The medical cost of this disease in the US is about $2.5 billion a year. This cost does not include the very real costs of pain, reduced mobility, reduce quality of life, and lost productivity.

E. Participant Contribution

XRT provided full CRADA funding.

XRT fully participated in the development and demonstration of the prototype units and the associated measurements.

F. Documents/Reference List

F.1 Project Abstract:

LLNL and IIC, which became XRT and is now Medtronic, entered into a CRADA for the development of an x-ray catheter. The following tasks were accomplished under the CRADA: the modeling and experimental testing of several candidate geometries, the development of microfabrication techniques for the electrical and vacuum components, the modeling and experimental measurement of the thermal loading produced by the x-ray catheter, and the fabrication and demonstration of prototype x-ray catheters. This was accomplished in a 13-month period beginning in March 1996 and ending in April 1997.

F.2 Weekly Reports:

Weekly reports have been sent to XRT previously.

F.3 Final report:

A three-volume final project report has been sent to XRT previously. The final project report includes all weekly reports previously submitted to XRT.

F.4 Intellectual Property:

a) Participant option to license CRADA Intellectual Property:

Under Appendix C, "Intellectual Property Agreement," the exclusive period reserved for Participant to negotiate a license to Intellectual Property first arising or produced under this CRADA is for the life of the CRADA plus a period of not more than six (6) months after the completion or termination of the CRADA. Appendix C also provides that any license granted to Participant will be based on reasonable commercial terms.

By letter dated April 17, 1997, Participant XRT notified The Regents of its intent to terminate the CRADA. The Regents notified XRT that full payment for all work done through the date of notice of termination is required before the CRADA can be terminated. XRT committed to making such full payment by June 30, 1997, at which time the CRADA would terminate. The final payment was received from XRT on July 9, 1997.

b) CRADA Intellectual Property:

XRT Sole Subject Inventions: None

Joint LLNL/XRT Subject Inventions:

IL-10146A

LLNL Sole Subject Inventions:

IL-10164

Under Article XV of the CRADA, if a Party elects not to retain title to any invention made by its employees, the other Party has second option to elect to retain title to the invention.

LLNL Copyrightable drawings:

Numerous technical drawings were developed. A copy of these drawings was transmitted to XRT in Volume III of the project report.

F.5 Financial Accounting:
LLNL provided to XRT an accounting of funding money spent before the termination of the CRADA on April 17, 1997. The Parties agree that LLNL will refund to Medtronic $17,043.72 in unspent funding provided by XRT for LLNL work on the project.

G. Acknowledgement

Participant's signature of the final report indicates that, to the best of its knowledge:

1) Participant has reviewed the final report and concurs with the statements made therein.
2) Participant agrees that any modifications or changes from the initial proposal were discussed and agreed to during the term of the project.
3) Participant certifies that all reports either completed or in process are listed and all subject inventions and the associated intellectual property protection measures generated by his/her respective company and attributable to the project have been disclosed or are included on a list attached to this report.
4) Participant certifies that if tangible personal property was exchanged during the agreement, all has either been returned to the initial custodian or transferred permanently.

Medtronic cannot certify that proprietary Participant information has been returned or destroyed by LLNL.

6/12/01
Mark Schlossberg Date
Medtronic AVE

7-3-01
James Trebes, LLNL PI Date
Lawrence Livermore National Laboratory

Attachment I: Discussion of Noncrimp-off Fabrication Techniques

Discussion of Noncrimp-off Fabrication Techniques
Attachment I
CRADA No. TC-1265-96

Date: May 26, 2000 Revision: 0

It is the recollection of the LLNL Principal Investigator that discussions were held between the Parties related to non-crimpoff techniques as well as crimpoff techniques for fabricating x-ray emitters. The Parties understood that the crimp-off configuration was pursued as an interim lower cost expedient for near term progress, and the final version would incorporate a noncrimp-off design. The project was put on hold before any emitters with the noncrimp-off configuration were fabricated.

Medtronic AVE has reviewed reports and other documentation associated with the project, and has been unable to confirm that such discussions took place or that the intent of the Parties was to ultimately produce an x-ray emitter incorporating noncrimp-off fabrication techniques.