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Final Report Certification

for

CRADA Number 99-0558

Between

UT-Battelle, LLC

and

ISOTRON, INC.

(Participant)

(OF NORCROSS, GA)

Instructions:

Mark the appropriate statement in 1a or 1b below with an "X." Refer to the articles in the CRADA terms and conditions governing the identification and marking of Protected CRADA Information (PCI).

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2. The final report does not contain Proprietary Information.

3. By the signature below, the Participant has no objection to the public distribution of the final report due to patentable information.

For the Participant:

ROBERT W. EBLING III

(Name)

PRESIDENT + CEO

(Title)

JUNE 27, 2007

(Date)

CRADA Final Report

CRADA No. ORNL99-0558

Development of Californium-252 Miniature Source Assemblies

PROTECTED CRADA INFORMATION

This report contains Protected CRADA Information which was produced on June 26, 2007 under CRADA No. ORNL99-0558 and is not to be further disclosed for a period of 5 years from the date it was produced except as expressly provided for in the CRADA.

June 26, 2007

Development of Californium-252 Miniature Source Assemblies

CRADA No. ORNL99-0558
with Isotron, Inc.

CRADA Final Report
June 26, 2007

Abstract

The purpose of this CRADA between ORNL and Isotron, Inc. is to develop miniature californium-252 sources configured for remote handling that can be used in neutron brachytherapy for treatment of cancer. Brachytherapy places the radioactive source at or near the site of the tumor, using a catheter. The CRADA ran from late 1999 through November 2005.

The heart of a Cf-252 source is the radioactive core wire, which is sealed inside a metallic source capsule. Previous Cf-252 medical sources were based on a cermet wire with californium oxide dispersed in palladium, typically >1-mm diameter and <0.1% Cf-252 by weight. Previously, the standard medical source in the U.S. was the Applicator Tube (AT) source, 23-mm long, 2.8-mm diameter, with ~30 μg of Cf-252, and which required manual loading into patients by medical staff. The goal of this work was to develop capabilities and technology to fabricate higher-intensity Cf-252 sources attached to a positioning cable, with overall diameter approaching that of existing photon (iridium-192) brachytherapy sources (i.e., ~1.1 mm).

This work was successful in developing and demonstrating new technologies and procedures for the fabrication of miniaturized Cf-252 sources. CRADA-designed equipment reduced the wire diameters significantly (patent pending). Short wire segments were cut and successfully welded inside capsules meeting the miniaturization goals. A batch of seven prototype sources was prepared that met fabrication specifications. Although their neutron emissions were not maximized, they were still several times more intense than the previous AT sources. Very robust source-to-cable attachment methods were demonstrated (patent issued). A shipping canister was designed and built to contain the completed source assembly. Isotron designed and built a computer-controlled remote afterloader system to deliver the new sources for treatments.

Statement of Objectives

The technical objectives of the CRADA were to:

1. Fabricate thinner, higher-intensity Cf-252 core wires.

2. Develop capsule designs which:
   a. Can accommodate these Cf-252 core wires,
   b. Are amenable to closure by welding, attachment to delivery cable, and decontamination within the radiological hot cells. Decontamination involves removal of transferable radioactive contamination until wipes of the exterior surfaces do not contain measurable activity above the limits required for transferable radiological controls.

3. Design, fabricate, and demonstrate techniques and systems for:
   a. Cutting of short core wires and insertion into capsules,
   b. Capsule handling and welding,
   c. Attachment of capsule to delivery cable,
   d. Decontamination of source assemblies, and
   e. Packaging of source assemblies into shielded shipping containers.

The primary goal of this CRADA was to develop more flexible neutron source geometries and intensities, to permit simplified source handling with reduced radiation dose to medical personnel, and more effective treatment of cancers.

Benefits to the Funding DOE Office's Mission

The U.S. Department of Energy Isotope Programs sells the californium-252 radioisotope for commercial applications. Historically, californium-252 sales generate between $1M and $1.5M annually for the Isotope Programs budget (sales of 20 to 25 mg of Cf-252). Development of a commercial product as a result of this CRADA, with each treatment unit projected to require hundreds of micrograms of Cf-252, would have a significant positive impact on Isotope Programs revenues. The projected application of this commercial product could establish a major new growth market for Cf-252 sales. Isotron's application of this technology to cancer therapy would highlight the humanitarian goals of the Isotope Programs.

Work Performed by All Parties

Work under this CRADA was primarily performed within the Californium Facility (CF), Building 7930 of the Radiochemical Engineering Development Center (REDC) at ORNL. The CF is a specialized hot cell facility dedicated to the purification of Cf-252 and its encapsulation and storage, as well as the packaging and shipment of sealed Cf-252 sources. Both contaminated and uncontaminated hot cells and associated infrastructure are uniquely adapted for Cf-252 handling.

1. ORNL implemented and demonstrated improved Cf-252 core wire fabrication techniques, developing the techniques and hardware to increase the Cf-252 content of the wire while decreasing the minimum achievable wire size.

For this effort, Isotron supplied or funded all materials and hardware, fixtures, tooling, camera and monitors, etc. required for the development of these improved techniques for the fabrication of core wires. ORNL provided work space for developing the manufacturing processes and demonstration of radioactive core material fabrication. ORNL provided all labor for the development and fabrication of prototype core wires, completed required safety documentation for new and modified processes and hardware within the CF, and developed operating procedures for prototype core wire fabrications and handling.

2. ORNL developed the capability to fabricate miniature Cf-252 sources and source assemblies (i.e., a source attached to positioning cable) for remote handling of the source.

For this effort, Isotron designed, supplied and/or specified the materials and components (capsules, cables, etc.) used in prototype source fabrication in the hot cells and testing outside the hot cells. Isotron supplied or funded hardware, welder, camera and monitors, etc. required for the fabrication of sources beyond that used routinely within the Californium Program. Isotron specified the requisite testing to address safety issues of weld integrity and reliability of cable-to-capsule attachment, and procured or designed testing equipment as needed. Isotron supplied the engineering drawings for capsule designs. Isotron designed and built the computer-controlled remote afterloading system to deliver the sources for treatment, and designed a shielded storage container for the sources when not in use.

ORNL provided work space for manufacturing and testing of prototype and radioactive sources and assemblies, and storage of radioactive sources after fabrication. ORNL provided all labor for the development, testing, and fabrication of source and assembly designs. ORNL provided special form test results for demonstration of source design and fabrication integrity.

ORNL developed in-cell cable-to-capsule joining capabilities, designed and built packaging configurations for shipping the completed source assemblies, and provided assistance in planning for post-fabrication source assembly handling activities. ORNL developed required safety documentation for process and hardware modifications within the CF, and operating procedures for fabrication and handling of prototype sources and assemblies.

Subject Inventions

Patent ID #1288C:	Cable Attachment for a Radioactive Brachytherapy Source Capsule
Patent ID # 1289C pending:	Thin Californium-Containing Radioactive Source Wires

Commercialization Possibilities

This CRADA holds the potential for significant commercialization possibilities due to its promise of improved clinical outcomes for several types of cancer.

Plans for Future Collaboration

Isotron requested during the first quarter of 2007 that ORNL initiate a new CRADA for the fabrication of new sources for clinical testing, and is awaiting ORNL's processing of the request.

Conclusions

The effort to develop new technologies to permit fabrication of miniature, higher-dose-rate Cf-252 neutron brachytherapy sources was successful. A batch of miniature Cf-252 brachytherapy sources was fabricated containing a Cf-252 wire of smaller diameter but with greater Cf-252 volumetric loading than any neutron source previously fabricated by ORNL or anyone else. Although smaller in size, the first Isotron sources contained several times more Cf-252 than the previous standard AT sources. The technology to fabricate these thinner, higher-dose-rate wires was developed through this CRADA. A method of attaching the source to a positioning cable was developed that provided a very robust connection and permits computer-controlled remote afterloading and positioning during treatments. The methodologies to fabricate the thinner wires and to attach the source to a cable were both submitted as patents.

Plans for continuing collaboration between Isotron and ORNL is under continuing discussion, with a goal of implementing a new cooperative agreement for additional source fabrications and delivery to end-users.