Minimally Invasive Spatial and Temperature Control of Deep Tissue Heating

Submitted to Nine Sigma

November 30, 2012

By

Raymond Kasevich PE.

Dr Jeb Rong

JR Technologies LLC.

964 Main Street

Great Barrington, MA 01258

Overview of Proposed Technology

A miniature and flexible microwave antenna system as energy source with diagnostic capability for precise tissue heating, monitoring, and control is proposed. The basic antenna components are the result of years of development of miniature radiating elements using catheters by Kasevich in applications such as BPH and microwave balloon angioplasty and other large scale non-medical applications using radio frequencies .The shape and volume of the tissue to be heated is provided by the design of the antenna system with specific material properties to control the thermal pattern shape , depth of energy penetration, and temperature distributions at a given frequency. Control of volume temperature close to the energy source below 41 C is provided by separated but relatively localized energy sources. They electromagnetically focus separately on the target volume to achieve the desired temperature difference between the targeted volume and boundaries to insure no tissue damage to surrounding tissue.

The proposed miniature system will provide the required target temperature and energy delivery time and be capable of either non-invasive or minimally invasive application without damage to the surrounding tissue. Impedance spectroscopy methods will be employed for real time display and monitoring the volume tissue electrical impedance vs. frequency which depends on the volume size and temperature. Any measured volume or unwanted temperature deviation during treatment is immediately discernable based on a previously calibration of the tissue volume both in size and physical properties such as electrical conductivity and dielectric permittivity (dielectric constant).

A fiber optic temperature probe will an integral part of the antenna system to provide real time measurement of temperature between the target volume and energy source .The input impedance of the energy source target (antenna) will change with time and frequency and can be monitored and displayed by a portable network analyzer as contours of impedance vs. frequency which is the basis for impedance spectroscopy.

Experience with Proposed Technology

A compilation of a wide variety of microwave tissue heating applications by Kasevich et.al is summarized in the appendix. He has over 20 years of experience in these applications for both commercial system development and patents. They include design, experimentation and fabrication of various miniature microwave energy sources, and related equipment development. The most recent work was the development indicated in US Patents… related thermal microwave treatments for benign hyperplasia. This approach included using impedance and microwave tomography for diagnostics and control. Systems were developed for USSC and several other major medical equipment manufacturers

He began his early work related to the development of miniature microwave probes for the treatment of brain tumors. The patented designs involved a fiber optic core integrated with the microwave antenna to achieve simultaneous heat imagery with the treatment volume. A patent was issued.

Development work continued on using miniature antennas in catheter that could allow for both electronic beam steering and focusing energy without damage to surrounding tissue. A significant design goal in was the avoidance of heating tissue outside the target volume by both phased array techniques and simultaneous pattern thermal measurements.

Kasevich applied impedance measurement diagnostic techniques in benign prostatic hyperplasia or BPH using simultaneous miniature microwave rectal and urethra probes to define the overall induced thermal pattern in the prostrate. He was intensively involved with the laboratory testing and design of this system with patents issued (Appendix)

Kasevich was extensively involved at the Mayo Clinic (Kasevich, and Drs Schwartz and Viestra) to develop miniature and microwave probes for microwave balloon angioplasty. Tests were conducted under sponsorship of Bard management in Billerica Massachusetts at the Mayo Clinic in Rochester Mn.The goal was the ultra miniaturization of catheter with microwave probe to treat plaque in capillary vessels with a microwave probes and cable having a 5-10 cm turning radius and operate for 30 seconds with sufficient power delivery without overheat. A patent was issued.

A Radiofrequency ablation device prototype system was developed by Kasevich for the United States Surgical Corporation in Norwalk Connecticut and tested at Yale Medical Center in New Haven, Connecticut .A patent was issued.

A summary of many publications related to his work is attached in appendix with some of the patents issued.

The proposed technology meets the listed specifications in the following manner:

- *The proposed technology provides a focused and controlled thermal pattern from miniature microwave energy sources on a less than four millimeter flexible cable using pulsed microwave energy to avoid heat transfer from target volume.*
- *The miniaturized line source electromagnetically creates thermal energy based on tissue dielectric properties of target volume to achieve the desired temperature of 65 degrees in less than 2 minutes*
- *Separated sources allow temperatures between the source and targeted volume of 1 cubic centimeter not to exceed 41 C*
- *The sources are physically apart not exceeding 20 mm. on miniature microwave cable.*
- *No leakage of microwave. All source directed at target volume.*
- *The line source will not exceed 4mm in outside diameter.*
- *Fundamentally, by choice of type of antenna design and certain material parameters, frequency, and beam steering, a focused energy within the target volume at the desired temperature is achieved without damage to surrounding tissue. This miniature system can be catherized if required.*
- *Special fabrication techniques have been developed by Kasevich to achieve miniature and flexible coaxial cables for the transmission and delivery of microwave power*

More specifically, several miniature antenna elements that have a minimum near electric field structure will be design and tested as a phased array such that each element has minimum radiated power with appropriate time phasing to insure no thermal damage whatsoever to surrounding tissue but deliver the requisite heat load of 65C to the 1 cubic centimeter volume of tissue up to 10 mm from the energy source/ probe. Temperatures closer to or further from the energy source beyond the target volume will not exceed 41 C. The microwave power input will allow the precise target temperature of 65 C be achieved in less than 2 minutes with very moderate microwave power .

Kasevich has fabricated low cost, portable microwave sources that would be suitable for this application. Power dividing would be required to operate the system as a phased array. The power cables are miniature and flexible and can be specially fabricated with conductive coatings to achieve very small diameters and high bending radii. Several cables together would not exceed 4 mm outer diameter.

The cabling and antenna elements are simple to fabricate and represent low cost. They can be thrown away or discarded after usage. The microwave power source is comparable to the cost of a commercial microwave oven but not exceeding a few tens of watts of delivered output power into a 50 ohm load.

The impedance matching between the energy sources is important and is taken care of through choice of a specific antenna assembly matched to the tissue dielectric properties. This insures optimum coupling of power from the source to the 1 cubic centimeter volume. A fiber optic cable will be employed to continuously monitor temperature during radiation. Calibration of the antenna probe temperature will give the temperature of the target volume based on computer simulations of the heating pattern delivered by the phased array.

The proposed phased array microwave system of collinear radiating elements will occupy approximately a 2 to 5 centimeter section of cable on choice of frequency for proper focusing of the microwave energy to the target volume up to 1 centimeter away from the source.

This microwave application should involve low risk of complications without anthesia and with minimum discomfort with rapid patient recovery based on known applications of microwave hyperthermia in which somewhat lower target temperatures are deployed. However, normal clinical studies with the developed system are required to ultimately answer these questions.

It is anticipated that 100,000 units of the antenna/cable system or approximately 2000 per week is a realistic manufacturing goal with the appropriate facilities. Small microwave power supplies could also be manufactured at this rate at the same facility.

Advantages of Microwave Power Energy Source:

- *Is not as sensitive to variations in tissue density as in ultrasound applications.*
- *Selective heating of moisture in tissue target volume without excessive heat transfer by employing pulse power microwaves.*
- *The microwave antennas are their own diagnostic using impedance spectroscopy techniques to discern microwave energy absorption effects on tissue volume and antenna impedance equivalent to separately measuring tissue dielectric properties. These properties are sensitive to moisture loss and size of target volume.*
- *The electromagnetic wavelengths of microwaves in tissue are comparable to target dimensions. This comparison insures efficient use of the radiated power.*
- *Array techniques can be employed for precise focusing*
- *Electronic beam steering may be employed to more precisely target the volume to be heated.*
- *Selective heating since microwaves are principally absorbed by water.*
- *Pulsed microwaves minimize heat losses.*

- ***Microwave equipment is relatively cheap and easy to operate as compared to laser equipment.***
- ***Microwave energy can be used for multiple purposes: hyperthermia, ablation, coagulation, etc.***
- ***Minimum invasiveness.***

- ***Note that RF is too excessive in wavelength to concentrate energy efficiently in such a small target volume.***

- ***Low cost, small equipment size and portable. Easy to hand operate. No major capital equipment expense as with laser sources***

  .
- ***Heat mechanism requires no mechanical tissue damage. Simply heating conductive tissue with intrinsic water content to acquire short and rapid heating times. This is selective heating.***

- ***Phase 1 Design Requirement***

Statement of Work

The overall goal of this program is the development of a miniature and flexible microwave antenna array (cylinder or planar geometry) configured to not exceed 4mm in diameter and approximately 5 to 8 centimeters in length. The array will heat a target volume of 1 cubic centimeter to a temperature of 65 degrees C in less than 2 minutes. The distance from the array (energy source) is up to 10mm.The tissue surrounding the target volume will not exceed 41 degrees C. Thermal studies of microwave heat application using the proposed array will be conducted in phantom tissue.

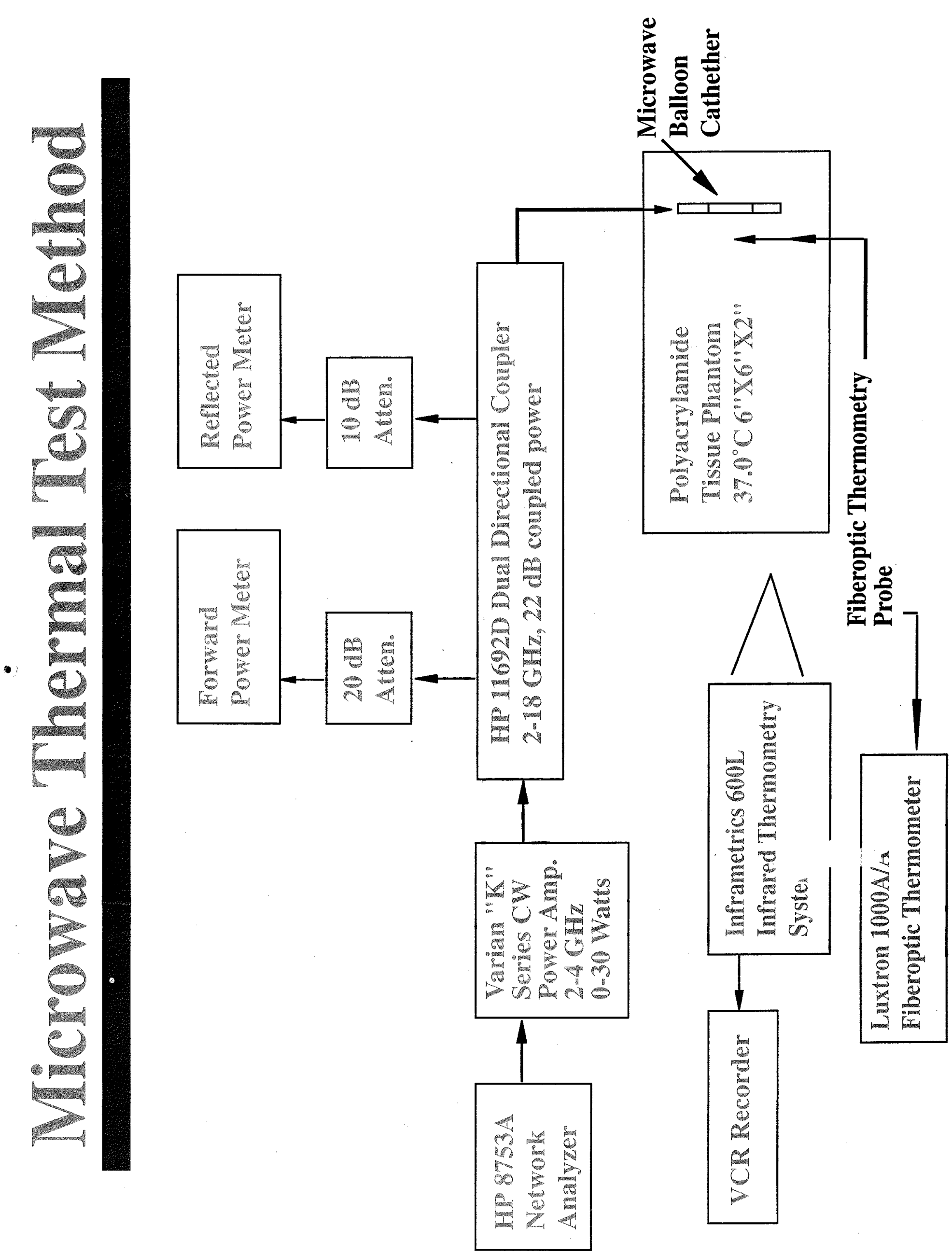
Task 1: Selected tissues will measured for their frequency and temperature dependent complex dielectric properties. The phantom material will be selected for testing based on these properties

Task 2: Microwave Antenna Array design. Existing designs developed by Kasevich will be tested in phantom tissue (polyacrylamide gel solution for example). Detailed computer analysis will be performed for the selected array to evaluate microwave heat distributions for the target volume and surrounding tissue. The power requirements and verification of array design will be determined from computer simulations before phantom load testing begins.

Task 3: Experimental Array Measurements. A test set-up will be designed and assembled. A basic set-up for microwave array testing in phantom tissue is shown in the following experimental equipment layout. Complete temperature, power input, temperature, array electromagnetic performance, and impedance (power efficiency) measurements will be taken with this type of set-up. These

measurements compared to the numerical simulations in Task 2 will provide the proof of concept of the proposed system and specifically demonstrate the controllability of the microwave heating to the target temperature of 65 C in the cubic centimeter volume without exceeding 41 degrees anywhere outside the volume during treatment time.

Task 4: Phase 1 Summary Report



Cost and Milestones for Phase 1

- ***Other Technologies:***
- ***Laser Surgery***
- ***Laser equipment expensive compare to RF***
- ***Bulky equipment***
- ***Strict safety precautions***
- ***May requirement multiple treatments***
- ***Difficult to avoid heating tissue between energy source and target volume***
- ***Acoustic Transducers***
- ***Onset of tissue damage can be unpredictable if cavitation (microbubbles) occurs. High temperatures inside the bubbles can form shock waves that can mechanically damage tissue.***
- ***Phased arrays can be employed for focusing as with microwaves. However, cavitation possibilities do not exist with microwaves because the heating mechanism with microwave is***

- ***Appendix (Selected US Patents)***

1. Microwave Therapy of Solid Neoplasms, S. M. Selikowitz (1) and R. S. Kasevich (2) - December 9, 2004.

2. Portable Microwave Control Unit Developed by CS Medical Technologies, LLC for ProUroCare 2000-2001.

3. Directional Heating Pattern of Patented Catheter Antenna System, CS Medical Technologies, LLC.

4. Early Prototype Antennas for Mayo Clinic and Albert Einstein College of Medicine at Montefiore Hospital in New York City, NY CS Medical Technologies, LLC.

5. Investigation of Microwave Heating. Presentation at American College of Cardiology, Atlanta, GA (1988-1989), Kasevich, Schwartz and Vlietstra.

6. Microwave Balloon Catheter for Benign Prostatic Hyperplasia, 12th Annual Meeting of the Society for Urology and Engineering, Inc., New Orleans, LA (12 April 1997) Kasevich, Selikowitz, LaCourse and Meyer.

7. Electromagnetic Scale Modeling of Implantable Microwave Antennas for Cancer Hyperthermia. 14th Northeast Bioengineering Conference, Durham, MA (10-11 March 1988). Kasevich.

8. Theoretical Basis for Electrosurgical Arc Discharge Characterization and Power Control. Surgical Applications of Energy Sources, Estes Park, CO (17 -19 May 1996). Kasevich and LaCourse (Paper and Presentation).

9. A Flexible, Miniaturized and Focused Microwave Antenna System for Medical Application. 1995 IEEE Engineering in Medicine & Biology 17th Annual Conference & 21st Canadian Medical and Biological Engineering Conference (20 -23 September 1995) in Montreal, Canada. Kasevich.

US

10. Mutual Impedance Coupled Microwave antennas for Thermal Treatment and Characterization of Solid Tumors. Kasevich.

11. End-Fire Catheter Antenna for Microwave Ablation of the Endocardium. Kasevich, Selikowitz, LaCourse and Smith.

12. Development of a Virtual Instrument for Control of Microwave Applicator for Medical Hyperthermia and /or thermotherapy. December 10, 1998, Great Barrington, MA. Kasevich, Price and Steffel.

13. Multiplexed Antenna Array for Solid Tumor Therapy. Small Business Innovation Research Program, Phase 1 Grant Application, (March 1, 1997- August 31, 1997) Kasevich.

14. Selected Patents.