Treatment of Solid Malignant Tumors with Microwave Balloon Ablation Catheters and Localized Chemotherapy


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Abstract — The paper describes a new approach to the treatment of solid malignant tumors. In this approach the tumors are thermally ablated with minimally invasive microwave balloon catheters, and the cavities created in the tumors by the balloon catheters are filled with anticancer agents that can be forced through the ablated malignant tissues to the margins of the tumors in order to destroy any remaining viable tumor cells. In vivo and in vitro experiments are described that illustrate the ability of microwave balloon ablation catheters to rapidly ablate of large volumes of tissues, to create reservoirs for anticancer agents in the ablated (necrosed) tissues, and to force substances with large molecular weights that are introduced into these reservoirs through the ablated tissues to the margins of the ablation.

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1. INTRODUCTION

Despite important advances in the treatment of cancer with surgery, radiation therapy, and chemotherapy, and despite the introduction of newer anticancer therapies such as, for example, hyperthermia and monoclonal antibodies, there still remains an urgent need for additional new therapies to help the numerous cancer patients that are failing currently available therapies.

Here we describe a new approach to the treatment of solid malignant tumors. In this approach solid tumors are first thermally ablated (necrosed) with minimally invasive microwave balloon catheters that can produce lesions that conform to the shapes of the tumors. Next the cavities that are created by the balloon catheter in the necrosed tumor tissues are filled with anti-cancer agents that are forced by applied pressure through the necrosed tumor tissues to the margins of the tumors where they can act against any remaining viable malignant cells that if not destroyed could lead to recurrences of the cancer. These agents can be heated to enhance their anti-cancer efficacy. If immunotherapeutic agents are introduced into the cavities it might also be possible to stimulate systemic anticancer effects against distant metastasis.

2. EXPERIMENTAL RESULTS

Microwave balloon ablation catheters were tested in vitro in beef liver and in vivo in the livers of pigs. The microwave antennas were coaxial gap antennas that were matched at 915 MHz. The catheters were 20 cm long with a diameter of 3 mm and with inflatable balloons at their end. They were cooled with circulating water that was also used to inflate the balloons. The balloons inflated to a predetermined diameter and shape and could produce the radial forces needed to create cavities in necrosed tissues. Tissue temperatures were measured with thermistors and a microwave radiometer. These tests demonstrated the following:

- Cylindrical shaped necrotic lesions with a diameter of 3 cm and length of about 4.5 cm can be produced in vivo in 3 minutes with 100 watts of 915 MHz microwave power without carbonizing any of the tissues surrounding the balloons. The cavities produced in the ablated tissues closely approximated the shape and size of the cylindrically shaped balloons used that had diameters of 1 cm and length of 6 cm. When fluorescent Dextran with molecular weights as large as 2,000,000 dissolved in saline was introduced into these cavities it could be quickly forced by applied pressure to the margins of the ablated tissues.
• It is possible with balloon catheters that incorporate microwave reflectors to preferentially heat tissues in only one direction. This feature makes it possible to safely ablate malignant tissues that are close to vital healthy tissues.

• Temperatures of ablated tissues can be measured with microwave radiometers by using the coaxial gap heating antennas of the ablation balloon catheters for receiving the microwave noise from the ablated tissues. The microwave radiometers used in the experiments have been described at a previous PIERS meeting [1].

3. DISCUSSION

The experimental results obtained with microwave balloon ablation catheters indicate that this form of thermal ablation has important advantages over thermal ablation using radiofrequencies (RF), an approach that is now in clinical use for ablating surgically unresectable tumors, particularly hepatic tumors [2–4]. Heating with RF tends to be non-uniform sometimes leading to rapid charring or vaporization adjacent to the electrodes which often adhere to the tissues making removal difficult. This non-uniform heating can cause incomplete destruction of the tumors. Increasing the heating power in RF catheters has limitations, because resulting vaporization, carbonization, and boiling increases the RF impedance of the tissues and reduces the distances of heating and therefore the extent of tumor necrosis. In contrast, microwaves can deeply and uniformly penetrate tissues and raise the temperatures of large volumes of these tissues to values that cause necrosis in very short times. This is of great clinical importance such as when ablating large or multiple liver lesions. Microwaves, unlike RF currents, can penetrate necrosed tissues and travel unimpeded through non-adhering plastic balloons, and the microwave antenna used in the balloon catheters can be used to not only transmit heating power into the tissues but also to receive thermal radiation from the heated tissues which can be translated to average tissue temperatures by microwave radiometers.

For the same microwave power and duration, microwave balloon catheters can ablate larger volumes of malignant tissues than similar microwave catheters not equipped with balloons. This is because the expanded balloons compress the malignant tissues resulting in a reduction of blood flow and in the distance microwaves have to travel inside the tumors in order to ablate a given volume of tumor. Heating with balloon catheters is also more uniform because the microwave powers emitted by the antennas spread in the balloons before reaching the tissues that are to be ablated, and because of cooling of tissues adjacent to the balloons. Balloons prevent sticking of the catheter to ablated tissues, can be tailored to ablate special shapes, can ablate tissues omni-directionally as well as in one direction only and most importantly, the expanded balloons create cavities in the ablated malignant tissues that can be filled with anticancer agents for localized chemotherapy.

What are the unique features of the microwave balloon ablation/localized drug delivery approach?

• Technically very simple. The cavities that are automatically created by thermally ablating tumor tissues with microwave balloon catheters serve as reservoirs for drugs for attacking any remaining viable cancer cells at the margins of the tumors and also for stimulating systemic immune responses.

• No limitations on the type of drugs that can be introduced into the reservoirs.

• Different drugs can be introduced either together or sequentially.

• Drugs in the reservoirs can be easily heated. This is a very valuable feature since raising the temperatures of a number of commonly used chemotherapeutic agents above core temperatures significantly increases their anticancer activity. Examples of such agents include bleomycin, adriamycin, and Cis Platinum.

• The margins of the ablation can be kept at elevated temperatures by continuing to heat after the ablation has been completed and the cavity has been filled with drugs. This further increases the local toxicity if agents such as bleomycin are used without increasing systemic toxicity.

• The rate at which drugs are forced through the ablated tumor tissues to the margin of the ablation can be controlled by amount of external pressure that is applied to drugs in liquid solutions.

• Drugs in slow-release form can be used to attack tumor cells over long periods of time. Suitable slow-release substrates would be drug-eluting polymers that are fabricated in biodegradable form.
REFERENCES