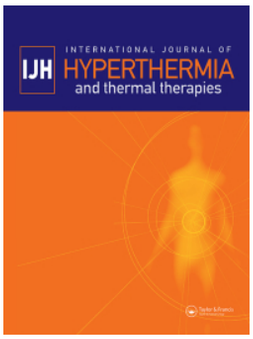

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Thermal tumour ablation: Devices, clinical applications and future directions

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Abstract
Tumour ablation is clinically applied mainly for non-operable liver tumours, with increasing application to other organ sites like kidney, lung, adrenal gland and bone. Most current devices use radiofrequency (RF) current to heat tumour tissue surrounding the applicator, which is introduced into the tumour under imaging guidance. Tissue temperatures in excess of 100°C are achieved, with cell death due to coagulative necrosis occurring above 50°C. Limitations of current ablation devices include inadequate imaging, limited size of coagulation zone and reduced performance next to large vessels. This paper reviews current interstitial RF and microwave devices, clinical applications and future research directions in the field of high-temperature tumour ablation.

Keywords: *Cancer, tumor ablation, radiofrequency ablation, microwave ablation*

Introduction

Tumour ablation has been rapidly accepted in clinical practice in recent years for treatment of liver cancer, with increasing application to other organ sites. This paper will describe interstitial radiofrequency (RF) and microwave devices, principles and clinical applications of high-temperature tumour ablation therapy.

Devices and principles

Tumour ablation devices generally consist of an applicator (catheter) that is introduced into the tumour under imaging guidance (see Figure 1). Energy deposited by this applicator results in heating of the surrounding tissue. The SAR (specific absorption rate) is only significant very close (within a few mm) to the applicator and—contrary to many

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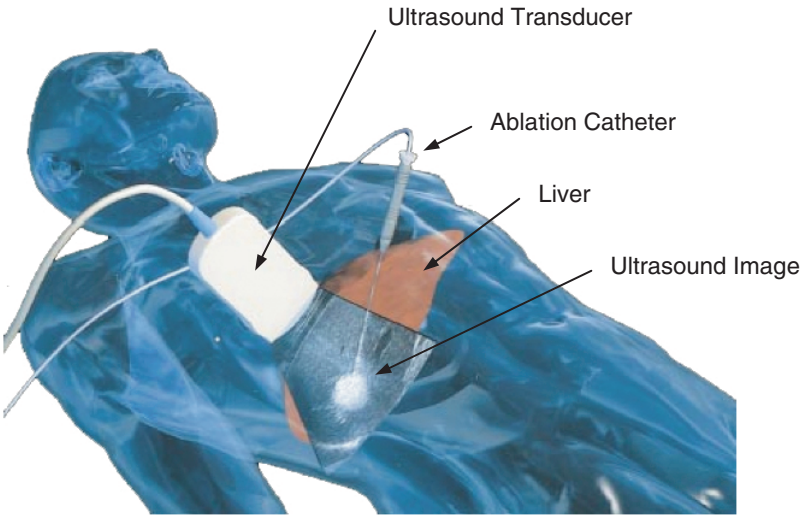

Figure 1. Patient set-up for liver tumour ablation using the percutaneous approach. The ablation applicator is inserted into the liver tumour through a small incision in the skin. Ultrasound imaging is used for guiding the electrode into the tumour and monitoring the ablation. The white region in the overlaid ultrasound image represents areas of gas bubbles due to high temperatures. Reproduced with permission from Dodd et al. [1].

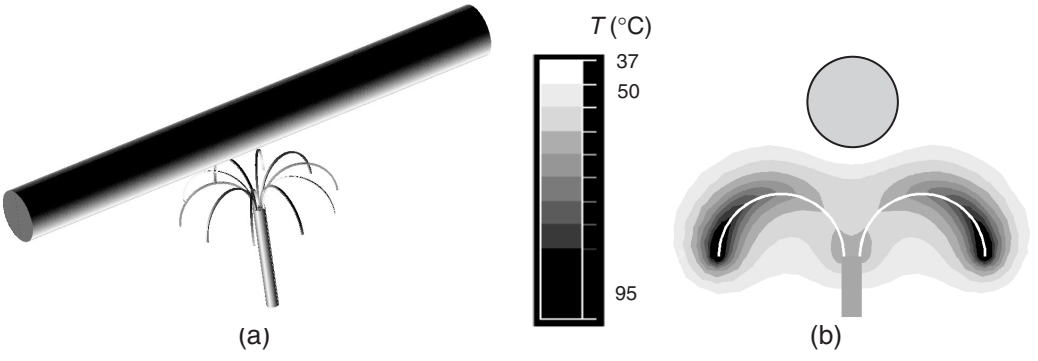

Figure 2. (a) A multi-prong electrode (30 mm diameter) is placed next to a large (10 mm diameter) vessel. (b) Typical tissue temperature profile at the end of 12-min ablation procedure in plane perpendicular to vessel axis, with coagulation zone border corresponding to the outermost gray boundary (i.e. 50°C isotherm). The vessel (grey circle) deflects the coagulation zone and prevents adequate heating close to the vessel wall.

hyperthermia devices—most of the tissue is heated mainly by thermal conduction from the hot region near the applicator (see Figure 2).

During tumour ablation, tissue is heated to temperatures in excess of 100°C. Cell death results from coagulative necrosis, which occurs above 50°C after ~2 min. The goal is to ablate the tumour plus a 1 cm margin of surrounding normal liver tissue. Studies have shown that the chance of local tumour recurrence increases with a smaller margin. Current ablation devices can create coagulation zones of 3–6 cm in diameter, i.e. for large

tumours (>3 cm) multiple overlapping zones of ablation have to be created. Most devices only support a single applicator making sequential ablations necessary [1].

The majority of tumour ablation devices currently in clinical use employ radiofrequency (RF) heating. RF current (typically 450–500 kHz) is applied to the active part of the applicator (electrode), resulting in frictional heating due to ion movement (i.e. electrically resistive heating). Above ~100°C, tissue vapourizes and can carbonize, preventing further heating from RF current. A major limitation of RF devices is performance next to large vessels that carry heat away and prevent adequate heating (see Figure 2). In a continuing effort to increase size of coagulation zones, newer devices employ saline infusion [2], multiple electrodes [3] and bipolar electrodes.

Recently, microwave ablation devices have emerged on the US market, where the applicator is an antenna that emits microwaves (typically 915 MHz or 2.45 GHz) into the tissue. Microwaves excite polar molecules (mainly H_2O), resulting in heating. Microwave devices have the advantages of higher tissue temperatures, since they are not limited by vapour formation, resulting in shorter application times than RF devices. Furthermore, preliminary results suggest they may perform better close to large vasculature compared to RF devices [4].

Clinical applications

Thermal tumour ablation has been most commonly employed for the treatment of liver tumours, but interest is growing for tumours in the kidney [5], lung [6, 7] and musculoskeletal system [8, 9]. This section gives a brief overview of the use of clinical RF devices for thermal tumour ablation in these organ systems to date.

Liver

A variety of conditions in the liver are being effectively treated with tumour ablation including: Primary liver cancer (hepatocellular carcinoma) in cirrhotic patients [10], metastatic colorectal cancer in non-operative patients [11] and symptomatic neuroendocrine (hormone secreting) tumours [12]. Ablation is contra-indicated in the presence of extra-hepatic disease. Tumour size, location and number are important factors affecting local recurrence rates. Recurrence rates are higher for tumours greater than 4 cm in diameter [13]. Furthermore, the perfusion-mediated cooling can spare perivascular tumour and negatively impact treatment success [14].

Liver RF ablation is a relatively safe procedure, with an overall mortality rate of ~0.3% and major and minor complication rates of ~2% and 5%, respectively [15]. Promising long-term survival data is becoming available. For example, the 3- and 5-year survival rates of patients with primary liver cancer were 78 and 54%, respectively [16], similar to conventional surgical resection. However, more long-term data and larger, randomized trials are needed to further define the role of tumour ablation in treating liver tumours.

Lung

Early experiences using RF ablation to treat primary and secondary lung tumours have been reported [6]. In the largest series to date, complete tumour necrosis was achieved in 91% (90/99) of tumours and no patients died from progression of thoracic lesions with a mean follow-up of 7 months [17]. Full coverage of the tumour was generally achieved, with complete coverage more likely for smaller, more peripheral tumours. The rate of minor

complications (small pneumothorax, pleural effusion or haemorrhage) was less than 30%. The rate of pleural effusions requiring drainage was less than 20%. Major complications have been rare, but include massive pulmonary haemorrhage and death. Optimization of equipment and algorithms for an aerated environment will likely further improve the safety and efficacy of lung tumour ablation.

Kidney

Renal tumour ablation is considered an effective, safe procedure. Indications include a prior partial or total nephrectomy, pre-existing renal insufficiency, various co-morbidities making the patient a high surgical risk or syndromes with multiple tumours. The retroperitoneal location minimizes the risk of major bleeding, while the exophytic (peripheral) location of many renal tumours decreases the chances of injury to the central collecting system. Central tumours are difficult to treat due to the heat sink effect of large vessels. Minor or self-limiting haemorrhage is the most common complication. Major complications are quite rare, but include significant haemorrhage, transient pain, bladder outlet obstruction and ureteral stricture [18]. Large studies with long-term follow-up have not been published.

Bone

In the musculoskeletal system, tumour ablation has become a common treatment for osteoid osteomas (small benign tumours of bone that are often painful and usually occur in the extremities of children and young adults) and to relieve symptoms from painful bone metastases [8, 9]. Experience has shown improved pain and quality of life scores after ablation. Major complications are rare and the addition of methylmethacrylate cement can help minimize the risk of subsequent fracture.

Imaging

Tumour ablation with interstitial devices can be performed as an open procedure, laparoscopically or percutaneously (i.e. minimally invasive through a small incision in the skin). Open surgery and laparoscopy are performed by surgeons, while interventional radiologists use the percutaneous approach. Ultrasound, Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) are used to guide percutaneous procedures, with CT and ultrasound being the most widely used modalities. While ultrasound offers real-time guidance, it cannot be used in the lung and can only be used to approximate the ablation zone margins by showing regions of high temperature where microbubbles have formed. Contrast-enhanced CT and ultrasound allow physicians to check for viable tumour immediately post-ablation [19].

Future applications

Thermal tumour ablation is also widely used to treat prostate cancer and is being investigated for several other malignancies, including medullary carcinoma of the thyroid, primary breast tumours and adrenal neoplasms.

Future research in tumour ablation will likely aim to alleviate existing shortcomings by:

- Improving imaging;
- Increasing coagulation zones; and
- Improving performance close to vasculature.

For example, ultrasound contrast agents can be used to visualize the devascularized coagulation zone by employing microbubbles to image perfusion. These agents are already available in other parts of the world and may become available in the US in the near future. Ultrasound elastography and MR thermometry are two other imaging techniques currently under investigation. Ultrasound elastography correlates tissue elasticity with the zone of ablation and has recently been shown to more accurately determine ablation zone volume than conventional CT [20]. MR thermometry maps temperature changes based on proton resonance frequency shift.

Research from the hyperthermia field can often be directly applied to the outer treatment region, where temperatures between 43–50°C are present. Radiation and chemotherapy agents applied adjuvant to ablative treatment have shown to increase dimensions of cell kill by causing cell death at lower temperatures than ablation alone [21]. This is potentially important close to large blood vessels, making it easier to achieve therapeutic temperatures. An agent using liposomal doxorubicin is currently in a clinical trial, where temperature sensitive liposomes release the drug in the hyperthermic region.

In conclusion, tumour ablation has seen a rapid proliferation in recent years, with an estimated 70 000 procedures performed in 2004. Early long-term results are promising and further device improvements will likely facilitate tumour ablation's continued growth in the coming years.

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