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Tumour ablation: current role in the kidney, lung and bone

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Abstract

The last few years have seen a rapid expansion in the use and availability of ablation techniques with hundreds of papers published. Radiofrequency remains the front-runner in terms of cost, ease of set-up, versatility and flexibility but other techniques are catching up. Ablation with cryotherapy and microwave, which were previously only available at open laparotomy due to the large size of the probes, are now readily performed percutaneously, with a predictable reduction in morbidity. Ablation is now accepted as the first line of treatment in patients with limited volume hepatocellular carcinoma who are not candidates for transplantation. There is continuing debate in most other areas but the evidence is increasing for an important role in liver metastases, renal carcinoma, inoperable lung tumours and some bone tumours.

Keywords: *Tumour ablation; radiofrequency; microwave; cryotherapy; liver tumours; lung tumours; renal cell carcinoma.*

Technical developments

The last few years have seen a rapid expansion in the use and availability of ablation techniques with hundreds of papers published. Radiofrequency (RF) remains the frontrunner in terms of cost, ease of set-up, versatility and flexibility but other techniques are catching up. Ablation with cryotherapy and microwave, which were previously only available at open laparotomy due to the large size of the probes, are now readily performed percutaneously, with a predictable reduction in morbidity.

Cryotherapy offers the opportunity to monitor the ice-ball with ultrasound (US), computed tomography (CT) or magnetic resonance imaging (MRI). The edge of the ice-ball represents the 0°C isotherm. Cell death occurs around −40°C and this isotherm lies approximately 5 mm inside the ice-ball. More powerful microwave generators have been developed and active research into better impedance matching with specific tissues should result in improved performance.

Microwave has several theoretical advantages; it can be designed to share a spherical geometry with most tumours and has a more predictable dose–response curve. Simultaneous use of multiple energy sources (probes/electrodes) is now available in all the different technologies. Improvements in guidance include the development of real-time co-registration techniques, most commonly CT and US. Collateral injury has been reduced by the widespread adoption of dextrose isolation. Five percent dextrose is instilled into the area adjacent to the ablation to displace vulnerable structures, usually bowel, away from the ablation zone. A displacement of as little as 1 cm is enough to protect the bowel.

Specific applications

Ablation is now accepted as the first line of treatment in patients with limited volume hepatocellular carcinoma (HCC) who are not candidates for transplantation. There is continuing debate in most other areas but the evidence is increasing for an important role in liver metastases, renal carcinoma, inoperable lung tumours and some bone tumours.

Tumours of the kidney

Nephron-sparing surgery presents a challenge to the surgeon. Yet, there is increasing evidence that even

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moderate degrees of renal failure can significantly affect survival following cardiovascular events. This will increase the focus of all physicians on the need to preserve renal function wherever and whenever possible. Local ablative techniques are the optimal nephron sparing treatment for small renal tumours. One study found that 95.2% of patients had a glomerular filtration rate (GFR) >60 ml/min per 1.73 m^2 at 3 years post RFA compared with 70.7% post partial nephrectomy and only 39.9% post radical nephrectomy[1]. Therefore patients with a solitary kidney and others with borderline renal function will increasingly be treated with ablation. Both tumour size and location are important predictors of outcome post ablation. Renal tumours up to 3.5 cm in diameter can be destroyed *in situ* by laser, RF or cryotherapy with virtually no damage to the surrounding normal renal tissue.

Some authors advocate cryotherapy for larger renal tumours <5 cm in diameter. Exophytic tumours are more readily ablated than central tumours. Multiple renal tumours are not rare and can be difficult to resect without complications but complications are rare after ablation, particularly if a percutaneous approach is used. Haemorrhage is the most common. Bowel injury can be prevented by dextrose isolation but it remains necessary to maintain a distance of >1 cm from the proximal ureter or cool the ureter via a stent as ablation can cause stricturing.

Several series have now been published including one retrospective comparison with partial nephrectomy which showed comparable oncologic efficacy albeit with a shorter mean follow-up in the radiofrequency group (30 months versus 47 months)[2]. An apparently promising meta-analysis was heavily skewed away from recent innovations by the inclusion of early technology, failure to analyse by tumour size and location, and the stipulation that success after a single procedure was the main endpoint[3]. Percutaneous ablative techniques are relatively easy to repeat compared with either surgery or laparoscopic cryotherapy. The question as to whether cryotherapy or radiofrequency is better is yet to be resolved and would be better addressed with mature technology and in a specific tumour cohort, e.g. tumours <3.5 cm.

Lung tumours

This is predicted to be the single largest growth area in ablation over the next few years. Laser, radiofrequency, cryotherapy and microwave have all been used. Currently the most widely used technique is radiofrequency. Good results can be achieved in small, peripheral tumours. Both inoperable primary and limited numbers of metastatic tumours have been treated. Computed tomography fluoroscopy facilitates electrode placement as small, scirrhous lung lesions can be difficult to penetrate with a larger calibre needle. The complication profile is well described. Pneumothorax occurs in about 40%, a similar incidence to that seen with trucut biopsy, but only a small percentage (10–15%) require drainage. The likelihood of a pneumothorax increases with the length of aerated lung that is traversed by the electrode and is more common when treating multiple tumours[4]. The second most common complication is pleural effusion. Other complications include infection, haemorrhage and bronchopleural fistulae. Infection is an unusual complication and in our series only occurred in patients with underlying asthma or chronic obstructive airways disease. Cavitation does not usually indicate infection but cavitating lesions are more likely to become infected.

During treatment a penumbra of ground glass opacification (GGO) develops around the tumour representing the ablation zone and a surrounding inflammatory reaction. Histological studies have shown that the zone of cell death lies 2–4 mm inside the outer margin of the ground glass shadowing. This has been corroborated in a clinical study, with >6 months follow-up, where the width of GGO at treatment was correlated with the development and location of recurrence. A minimum GGO of 4.5 mm is recommended to ensure complete ablation[5]. Over time the ablation zone becomes increasingly dense and then reduces in size. At 12 months, up to 33% of successfully treated small lesions will have shrunk to a linear scar. Recurrence is identified by enlargement of the ablation zone, or a change in the shape of the zone indicating enlargement in one area or the development of focal nodular enhancement. Tumours <3.0 cm can usually be ablated at a single session, larger tumours, 3.0–5.0 cm, may require more than one ablation or other additional therapy. Multivariate analysis has shown size to be the dominant feature determining complete ablation, but contact with >3 mm blood vessels or bronchi also increases the chance of recurrence[6]. Current indications include patients with small volume, but inoperable metastases and early primary lung cancer in medically inoperable patients. Early clinical studies report 3- and 5-year survival of between 46% and 57% in patients with colorectal metastases[7,8]. Combinations of radiotherapy and RFA have been used to good effect in primary lung cancer in inoperable patients[9]. Ablation is the best option for preserving lung function. The RAPTURE study showed that lung function recovered quickly after an initial immediate post-treatment reduction and was maintained at pre-treatment values 12 months later[10].

Bone tumours

One of the first accepted indications for ablation was the minimally invasive treatment of benign osteoid osteomas. Malignant primary bone tumours are usually treated by chemotherapy, radiotherapy and surgery. However, if aggressive therapy is delivered at an early stage, recurrence can be very difficult to treat. Treatment by RFA may be curative, but is more likely to form part of a palliative treatment regimen. CT or MR are the usual

guidance methods. Radiofrequency ablation and cryoablation have been advocated in the symptomatic palliation of bone metastases following radiotherapy. Initial results suggest that ablation can produce significant reductions in pain levels and analgesic requirements. Only limited numbers of metastases can be treated[11]. It is important to select patients with a clearly defined and understood dominant site of bone pain. Some authors promote the combination of ablation and cementoplasty, others argue that cementoplasty alone would be adequate. A trial to establish the relative merits of the two techniques has been suggested.

Conclusion

The last few years have seen a sharp increase in our understanding of ablation, maturation of the technology, an improvement in the safety profile, ablation efficacy and monitoring techniques and the publication of results in larger patient cohorts. Ablation will soon be sufficiently established to allow trials comparing ablation with conventional therapies in specific patient groups.

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