

## Editorial

# Ablative Therapy for Liver Cancer: Which?

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I am most grateful for the opportunity to reply to the editorial “The End of Cryotherapy for the Treatment of Nonresectable Hepatic Tumors?” (in this issue). This is real progress now that we are not arguing about ablation or not for liver tumor ablation, but rather about the type of ablation. Radiofrequency ablation (RFA) is undoubtedly an important treatment option, and it is much easier to use percutaneously, although it is yet to be established whether percutaneous RFA can achieve results as good as RFA or cryotherapy at laparotomy. Studies to date have tended to indicate that open RFA is associated with considerably better outcomes and that intraoperative findings alter the planned treatment in more than a half of cases.<sup>1</sup>

Cryotherapy is old and does not have much marketing muscle behind it. It requires a fairly complicated and expensive piece of equipment, but at least the systems that I have used have reusable probes. RFA probes are single use and cost approximately US\$1000. Cryotherapy has other advantages apart from the much lower recurrent costs: multiple probes can be used concurrently, which in patients with multiple lesions can significantly shorten procedure times<sup>2</sup>; the edge of a cryotherapy lesion is very easily seen on ultrasound, whereas RFA is much harder to see; and the use of edge cryotherapy is currently the only described method of achieving long-term survival in patients with involved margins at the time of liver resection.<sup>3</sup>

The safety of cryotherapy and RFA is, as with most invasive procedures, operator dependent. Although cryoshock (a multiorgan failure syndrome) has been seen with large-volume cryotherapy, particularly if twin freeze/thaw cycles are used,<sup>4,5</sup> it is also easy to avoid with a modicum of care and knowledge; our unit has not yet lost a patient from this.

The real issues have received remarkably little attention: Is RFA or cryotherapy more effective? Which is safer? Which is more practical? What are the costs?

The quoted comparison of intraoperative RFA or cryotherapy<sup>6</sup> was not randomized, but is a comparison of consecutive series, the second series (RFA) was associated with a lower morbidity and a lower recurrence rate (3 of 138 vs. 12 of 88). In a nonrandomized study, there are many confounding factors: Were the tumors comparable? Were there other improvements? I was most disappointed to find that my first 50 cryotherapy patients in Sydney did significantly worse than the second 50. The multifactorial reasons—including selection, technical and procedural skill, and probably other factors—make such a comparison between two different treatments very difficult. We certainly do see many local recurrences after RFA, and I am not convinced that there is any difference in recurrence rate compared with cryotherapy. The four RFA studies published before Pearson’s group<sup>6</sup> had RFA local recurrence rates of 50%, 50%, 90%, and 100%.<sup>7–10</sup>

The study by Adam et al.<sup>11</sup> of 64 patients treated by cryotherapy or RFA was dependent on the random availability of probe type. It is important to note that complication rates did not differ, but a higher rate of local recurrence (53% vs. 18%) was seen after cryotherapy. This small study, however, included both primary and secondary liver cancers, and there was no serious attempt to match groups for known

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prognostic variables for the outcome of ablative therapies—most importantly, the size of tumors and their proximity to large vessels.<sup>12</sup>

There are three controlled studies of RFA and ethanol injection for hepatocellular carcinoma, the most recent of which showed a significant survival advantage for RFA.<sup>13–15</sup> The lack of randomized clinical trials of ablation methods is very disappointing. In a State-funded hospital system such as ours, it is, however, difficult to obtain funding for single-use items, and the RFA companies have not produced any meaningful comparative studies. Why should there not be a randomized trial against cryotherapy? In a rabbit kidney cancer model, RFA and cryotherapy were equipotent.<sup>16</sup> In a porcine model of renal ablation, cryotherapy was considerably more effective and predictable.<sup>17</sup> No large-animal models of cancer allow meaningful comparison of RFA and cryotherapy, but there could be; it just requires effort. Perhaps cryotherapy is not dead. In fact, I used it today, and I would plead for some serious research.

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