Current Readings: Percutaneous Ablation for Pulmonary Metastatic Disease

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Percutaneous image-guided ablation is a technique for maintaining local control of metastatic lung lesions that may, in selected patients, confer a survival benefit over no treatment or systemic therapy alone. Although the currently accepted treatment for oligometastatic pulmonary disease is surgical resection, the existing body of literature, including the recent investigations reviewed within this article, supports a role for percutaneous ablation as an important and relatively safe therapeutic option for nonsurgical and in carefully selected surgical patients, conferring survival benefits competitive with surgical metastasectomy. Continued clinical investigations are needed to further understand the nuances of thermal technologies and applications to treat lung primary and secondary pulmonary malignancy, directly compare available therapeutic options and further define the role of percutaneous image-guided ablation in the treatment of pulmonary metastatic disease.

Semin Thoracic Surg 26:239–248

Keywords: lung ablation, lung metastasis, pulmonary metastasis, radiofrequency ablation, microwave ablation, cryoablation

INTRODUCTION AND GENERAL PRINCIPLES

The traditional treatment for metastatic cancer has been systemic medical therapy. However, for certain patients with metastases confined to one or few sites, termed oligometastatic disease, local means of controlling these sites of disease may prolong survival and palliate symptoms, and in some cases may result in long-term disease-free survival.[1] The treatment of oligometastatic disease to the lung demands a case-by-case, multidisciplinary approach. In properly selected patients without contraindications, surgical resection has generally shown the best long-term survival, with reported rates of 5-year survival in the range of 29%-48%.[2,3] Patients must have adequately preserved pulmonary function and be without other significant comorbidities that prohibitively increase operative risk. In addition, the extent of intrapulmonary disease must be such that the metastatic lesions can be resected while preserving enough uninvolved lung to maintain physiological function.

Percutaneous ablation is a minimally invasive technique for treating primary and metastatic lung tumors, based on the application of thermal energy to tissue through percutaneous probes, or applicators, placed into the lung under image guidance. Unlike surgical resection, there are no contraindications to pulmonary ablation based on pulmonary function tests. There is no defined maximum number of lesions that may be ablated, although ideal candidates for ablation will have 5 or fewer, and these lesions may be widely distributed through one or both lungs. There is likewise no well-defined limit on the number of times a patient may undergo pulmonary ablation, and the same lesion may be ablated more than once in cases of local recurrence. For a patient to undergo ablation with curative or life-prolonging intent, the lung should be the only or the dominant site of metastatic disease, and the primary site should be definitively controlled, most often by surgical resection.

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Ablation Modalities

Several ablation modalities are currently in use. For thoracic applications, all of them use computed tomography (CT) guidance to position one or more

1043-0679/$-see front matter
http://dx.doi.org/10.1053/j.semtcvs.2014.09.003

percutaneously inserted probes within or in close proximity to the target lesion. Once position is confirmed, thermal energy is applied to lung tissue with the goal of creating a zone of cell death that encompasses the tumor and a margin of surrounding lung, referred to as an "ablative margin." To date, there are no data directly comparing ablation modalities, and selection is largely based on operator and institutional experience.

The most often used and most well-studied ablation modality is radiofrequency ablation (RFA). This modality uses a metallic electrode to heat the target tissue by applying alternating current radiofrequency energy supplied by a generator, generally at frequencies 350-500 kHz. A grounding pad is placed on the patient's body as a reference electrode. Frictional motion of electrons near the ablation electrode produces heat. Temperatures greater than 60°C create instantaneous cell death. The size of the ablation zone is determined by technical parameters including the amount and duration of the stimulus, and characteristics of the tissue such as density and proximity to bronchovascular structures. Vascular structures near the target lesion can limit the effectiveness of RFA and all thermal-based ablation modalities due to the heat sink effect, whereby thermal energy is dissipated by flowing blood.

Cryoablation uses cold temperatures to create cell death by forming intracellular and extracellular ice, with resulting osmotic shifts that disrupt cell membranes.[4] Temperatures lower than −50°C are immediately cytotoxic. Commercially available cryoablation systems use pressurized argon gas to create low temperatures around a metal applicator probe through the Joule-Thomson effect. The resulting ice ball can be visualized on CT scans, allowing for real-time monitoring of the size of the ablation zone. The ice ball contains concentric ice spheres, or isotherms, with the lowest temperatures centrally immediately adjacent to the cryoprobe, graduating outward, and the highest temperatures at the periphery. Temperatures less than 20°C should extend past the target lesion by a margin of at least 7 mm, owing to incomplete cell death at the periphery of the ice ball. Various freeze-thaw schemes have been described in an attempt to maximize the efficacy of killing and the size of the ablation zone.[5] Generally, 2 or 3 freeze cycles are used with varying lengths of thawing in between cycles. Increased rates of post-procedural hemorrhage, which may be due to hypothermia-induced platelet dysfunction and lack of thermal coagulation effects, are one potential disadvantage of cryoablation. Injection of thrombin glue along the ablation tract may be performed to mitigate this risk.

Microwave ablation uses electromagnetic energy at significantly higher frequencies than RFA (900-2450 MHz in commercially available systems) to transfer kinetic energy to water molecules, resulting in tissue heating. Temperature rise is more rapid than with RFA, resulting in shorter procedural times, and the potential ablation zone is larger. Microwave ablation is thought to be less susceptible to heat sink effects than other thermal-based modalities, but does require a "choke" or cooling system within the antenna to minimize the risk of skin burns and nontarget ablation.

Laser ablation is a newer ablation modality that uses laser photons transmitted by a fiber optic cable to induce tissue heating. This modality is limited by charring of tissue around the fiber, which reduces the penetration of energy and limits the size of the ablation zone. This effect may be reduced using cooled applicator systems. Experience of published authors is limited, but a series of patients with thoracic malignancies treated with laser ablation has demonstrated favorable results.[6]

Irreversible electroporation is a non–thermal-based modality that uses direct electric current to induce poration of cell membranes, resulting in cell death by apoptosis. The technique preserves the collagenous architecture of the ablated tissue and may theoretically be safer than thermal modalities for lesions near mediastinal and hilar structures. It is not susceptible to heat sink effects. Although irreversible electroporation is being increasingly applied to solid abdominal organ ablation, it has not yet found robust application for lung tumors.

Recent Contributions to the Literature

Recent investigations have added to the growing body of literature supporting percutaneous ablation as a safe and efficacious modality for treating oligometastatic pulmonary disease in nonsurgical patients. Percutaneous ablation is a generally safe procedure, with low rates of serious complications. The largest single series of ablations to date, including 1000 procedures, was recently reported,[7] representing an important contribution to the procedure's published safety profile. In addition, several recent series of patients, representing the latest data on local recurrence rates and overall survival, have further reinforced the efficacy of percutaneous ablation in treating metastatic colorectal cancer,[8] metastatic sarcoma,[9] and all unselected pulmonary metastases.[10] Finally, 2 recent studies have attempted to characterize risk factors for local recurrence following percutaneous ablation.[11,12] These recent investigations are reviewed later, and their contribution to the body of knowledge concerning percutaneous