Breast Cancer Ablation: Imaging and Early Experience

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Summary. The goal of minimally invasive therapy for breast cancer is to eradicate cancer cells with minimal damage to the underlying normal breast parenchyma or skin. Tumor ablation is seen as a means of obtaining local control of breast cancer without surgery. Breast imaging is a critical component of therapy to (1) detect the primary tumor, (2) demonstrate the anatomical extent of the tumor, (3) Guide the tumor-ablative device, (4) monitor tissue effects during treatment, and (5) Monitor the long-term effects of treatment. Current protocols of minimally invasive ablation of primary breast cancer use physical means for tumor ablation. Preliminary data exist for the use of percutaneous excision and thermal energy (cryotherapy, interstitial laser photocoagulation, radiofrequency, and microwaves).

Key words. Breast, Cancer, Ablation, Ultrasound, Magnetic resonance

Introduction

The principles of breast cancer surgery underscoring removal of the breast and regional lymphatics originated in the late nineteenth century in Europe. Subsequently, Halsted proposed that breast cancer dissemination occurs sequentially involving the breast first, followed by involvement of lymphatics and regional progression that subsequently leads to systemic disease. This paradigm has served as a premise for surgical management of breast cancer during the past century [1].

Investigators from the NSABBP (National Study for Breast and Bowel Project) have questioned the validity of this concept with a series of prospective studies [2]. Current understanding of cancer biology suggests that systemic progression of breast cancer occurs early and independently from lymph node involvement.

As our understanding of the natural history and biology of breast cancer has evolved, the surgical treatment of breast cancer and local regional disease have also changed. Respect of patient autonomy in the decision-making process and the development of effective screening with mammography have contributed to a demonstrable change in breast cancer survival and clinical presentation. Cady et al. have

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documented a progressive decrease in the average size of breast cancer [3]. Subclinical breast cancer is currently a common presentation. This stage is defined as the detection of breast cancer before the development of any symptoms. Therefore, the management of breast cancer has evolved toward less invasive surgical treatment [2, 4]. The possibility of treating the primary tumor without surgery is currently the subject of several clinical trials [5].

Minimal Invasive Treatment of Breast Cancer (MITBC)

Definition

The effectiveness of breast-conservation therapy has been documented in multiple prospective clinical trials [2, 6]. Similarly, less invasive procedures of axillary staging are used commonly today [4]. Minimally invasive treatment is the next step in the evolution of management of breast cancer [5]. MITBC refers to local therapy without surgery and is the subject of ongoing investigation.

Principles

The ideal local therapy for breast cancer should eradicate cancer cells with minimal damage to the underlying normal breast parenchyma. Current local management of breast cancer requires wide local excision with negative margins [7]. Achieving pathologically negative margins may be challenging and may lead to repeat surgery and undesirable poor cosmetic outcomes. In spite of obtaining negative margins, adjuvant therapy (radiation) is required because the local recurrence rate is high with surgery alone [2, 6, 7]. Methods for percutaneous excision and breast cancer ablation seek to achieve the goal of targeted local cancer eradication without significant damage to surrounding tissues. Imaging guidance is essential to outline the diseased areas of the breast and direct the therapy.

Breast Imaging

The role of imaging in breast cancer minimally invasive treatment includes the following:

1. Tumor detection: magnetic resonance imaging (MRI) is the single most sensitive technique for diagnosis of breast cancer [8, 9]. However, MRI may not be superior to a combination of sonography and mammography [10]. The main limitation of MRI is its relatively low specificity and the difficulty in detection of in situ breast cancer [9, 10].
2. Determination of the anatomical pattern of spread is useful in patient selection and in planning ablative therapy. MRI is more accurate than sonography and mammography in the detection of a multifocal pattern of spread and multicentricity [11]. MRI is valuable in establishing the extent of disease, even in difficult scenarios such as lobular carcinoma [12] or intraductal cancer spread [13]. Breast sonography is less sensitive than MRI but is better than mammography.
3. Breast imaging is used as a guide to the percutaneous excision/ablative tool. Ablation devices have been guided with MRI [14], sonographic [15], and stereotactic

techniques [16]. Limitations to the use of MRI are the need of nonferromagnetic equipment and the cost and availability of the equipment. Sonography is widely available at a reasonable price and is highly accurate in the localization of tumors.

4. Real-time imaging for treatment monitoring is ideal. Real-time imaging enables adjustments of treatment parameters and targeting of multiple irregular areas in the breast. MRI is cumbersome because of the need of MRI coils for best imaging and the need of nonferromagnetic equipment. Ultrasound affords the highest versatility in targeting and monitoring. The use of ultrasound contrast agents may be helpful in the evaluation of tumor blood flow, which may be a primary endpoint of ablative techniques.

5. A combination of clinical assessment, breast imaging, and pathology may be important in the long-term monitoring of success or failure. A combination of these techniques seems more promising than the use of imaging alone. MRI may be able to distinguish necrotic, avascular tissue from viable tumor. Further experience is required in this field.

A combination of imaging techniques may provide the best outcome. Clinical examination, mammography, and sonography are useful for diagnosis of breast cancer. A combination of mammography, sonography, and MRI are needed for best assessment of the extent of disease. Patient selection is critical because cases of multicentric disease, extensive local or focal disease with Pagetoid spread, and those with large areas of ductal carcinoma in situ (DCIS) may be impossible to treat with focal ablative techniques. Sonographic guidance of the therapy is reliable, widely available, and affordable. Sonography may also be useful in the monitoring of therapy as a measure of blood flow. Long-term monitoring may prove to be difficult and may require tissue diagnosis of the residual abnormalities. Complete biopsy of the abnormality under ultrasound guidance may afford the only means of measuring the success of therapy.

Investigational Methods of Minimally Invasive Therapy

MITBC may be accomplished through percutaneous excision or tumor ablation with physical energy, generally extreme temperatures.

Percutaneous Excision

Advanced breast biopsy instrument (ABBI) is a procedure that mimics needle localized excisional biopsy but is performed under image guidance. In this procedure, the patient is placed prone on the stereotactic table and under compression; the location of the lesion is established by obtaining two stereo views on mammography. Using the Cartesian theorem, the location of the lesion is determined. A needle is then introduced into the target and a wire is deployed. A skin incision in the breast is required to advance the cutting mechanism of a cannula. A cylindrical specimen with a 2-cm diameter and of variable length can be removed. Assessment of the margins is possible. The major caveat is that the lesion is often located eccentrically and margins are involved in 60% of cancers excised with ABBI [17].

Vacuum-assisted core biopsy (VACB) is commonly used for diagnosis of breast lesions. Using stereotactic or ultrasound guidance, the vacuum-assisted core device can be guided to the breast abnormality allowing for extensive tissue sampling. Lieberman et al. [18] reported that calcific lesions were completely removed in 51% of cases. Gajdos et al. [19] reported that no cancer was found on the reexcision specimen in 17% of cases who underwent VACB for diagnosis. More recently, Fine et al. [20] have reported that benign palpable masses can be removed with a success rate of 99%. This result raises a possibility of its use directed at the treatment of breast cancer. With the vacuum-assisted core biopsy, a tumor can be removed in pieces, retrieving tissue samples of approximately 100 to 150 mg per sample. The success of this approach in the management of breast cancer has not yet been reported.

Tumor Ablation

Cryotherapy with liquid nitrogen as developed for the treatment of nonresectable liver has reported on the treatment of 16 patients by generating an iceball with a diameter of 28 mm. Complete tumor ablation was achieved in 5 tumors less than 16 mm in size. However, there was residual in situ carcinoma. Tumors larger than 16 mm had evidence of incomplete necrosis [21]. The freeze ball is highly anechoic on sonography, but assessment of the tissues deep to the freeze ball is impossible. Animal studies have documented the presence of residual cells in the frozen tissue.

Interstitial laser photocoagulation (ILP) uses a fiberoptic probe to conduct laser energy. The energy delivered causes hyperthermic ablation. Dowlatshahi et al. [16] have reported complete ablation in 70% of cases treated with ILP. A tissue temperature of 60°C and energy of 2500 joules/ml of tumor are predictors of successful ablation.

Radiofrequency ablation (RFA) was also developed for the treatment of nonresectable liver metastases. Cell death is secondary to dessication, denaturing of cytoskeletal proteins, and destruction of nuclear structure in the treated area. The size of the ablation field is determined by physics of resistive heat generation, requiring an array of conductors to deliver the thermal energy to a broad area. Izzo et al. [22] have reported on the results of a phase I study of 27 patients with a mean tumor diameter of 1.8 cm. Complete tumor ablation was seen in 96% of patients.

Focused microwave phased array ablation (FMPA) uses two opposing microwave applicators to generate microwave energy that produce deep tissue heating when properly focused. In a multicenter phase I study [15], we reported variable degrees of tumor necrosis in 68% of patients. Tumor necrosis was seen in 87% of patients receiving the highest dose in this dose escalation trial. However, patients with complete tumor ablation had residual DCIS.

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