

High-intensity Focused Ultrasound for the Non Invasive Treatment of Breast Fibroadenoma in Bangladesh

Nasrin Akhter¹, Md. Nurunnabi Mollah², Kaniz Fatema³ and Zubair Ahmed Ratan⁴

¹Asst. Professor, Dept. of Biomedical Engineering, Khulna University of Engineering & Technology, Bangladesh

²Professor, Dept. of Biomedical Engineering, Khulna University of Engineering & Technology, Bangladesh

³Department of Virology, BSMMU, Dhaka, Bangladesh

⁴Lecturer, Dept. of Biomedical Engineering, Khulna University of Engineering & Technology, Bangladesh

nasrin_dr@yahoo.com*, nurunnabim12@gmail.com, fatemadr.kaniz@yahoo.com, ratandmck62@gmail.com

***Abstract-**Breast fibroadenoma are benign (tumor) lesions which occur in about 10% of all women. Due to lack of breast cancer awareness in Bangladeshi population and inadequate knowledge of health care and ignorance, the majority of the patients are diagnosed at the advanced stage of the disease. Common treatment options for breast cancer include surgery, radiation, chemotherapy, hormone therapy, pharmacologic therapies. Typical treatment regimens can involve combinations of several options. The current clinical management of localized breast tumor is breast-conserving therapy. Clinical use of ultrasound in cancer is not only for the diagnosis but also for the treatment. Focused ultrasound offers a potentially non-invasive alternative to surgical lumpectomy. High-intensity focused ultrasound (HIFU) is a type of noninvasive, local ablation therapy in which external ultrasonic energy is transmitted into a lesion using an extracorporeal approach, leading to coagulative necrosis of the tumor. Hence, targeted lesions are completely destroyed, leaving the skin intact. The main mechanisms of HIFU ablation involve mechanical and thermal effects. Recent advances in HIFU have increased its popularity. Some promising results were achieved in managing various malignancies, including pancreas, prostate, liver, kidney, breast and bone. Other applications include brain tumor ablation and disruption of the blood-brain barrier. With increased precision, focused ultrasound has the potential to be a more effective lumpectomy than surgery. Thus it could potentially be a primary treatment approach for some patients. The aim of this study is to establish a non invasive treatment for breast tumor by High intensity focused ultrasound in Bangladesh.*

Keywords: Breast fibroadenoma, HIFU, Carcinoma, and Diagnosis

1. INTRODUCTION

Breast fibroadenoma are solitary, smooth, mobile benign breast (tumor or lump) lesions that can occur at any age but Usually occurring in women under the age of 30, they are seen in approximately 10% of all women during their lifetime [1, 2]. Breast fibroadenoma consist of combined proliferation and epithelial and fibroblastic tissue elements which are oestrogen-dependent and slowly growing [3]. Breast tumor are usually diagnosed by standard triple assessment which entails a physical examination, imaging by ultrasound and/or mammogram and if the patient is 25 years or older, a cytological or histological conformation of the diagnosis [3, 4]. The widespread implementation of routine screening mammography has resulted in the fact that benign breast diseases represent a growing percentage of pathological findings. Management of non-symptomatic breast lump is conservative once definitive diagnosis is made [4]. Management of symptomatic breast lump consists of conservative treatment, surgical excision or

vacuum-assisted mammotomy (VAM). Transformation from fibroadenoma to cancer is rare; regression or resolution is frequent, supporting conservative approaches to follow-up and management. All of cancers breast cancer is the most in Bangladesh and 2nd in the world deathful disease. World Health Organization (WHO) says that the death rate of breast cancer is high in Bangladesh and ranked Bangladesh 2nd deathful country in the world for breast cancer of women [5]. Most of the women in our country don't know about breast cancer before affected for a long period of time. Treatment of breast lump depends on the type of lesion and the stage of breast cancer. According to breast cancer stage there are different kinds of treatment. Treatment for breast cancer depends on the type and stage of the disease, the size the tumor, general health, medical history and age of patients. In most cases, the goal of treatment is to remove or destroy the cancer completely. Most breast cancers can be cured if found and treated early. Breast-conserving therapy (BCT), i.e. lumpectomy with additional

radiotherapy, is currently standard-of care in patients with early-stage breast cancer and has shown equal survival rates compared to radical mastectomy [6, 7]. Because of its superficial location, breast FA is especially suitable for minimally invasive ablation techniques. These techniques can be divided into heat-based modalities, which include high-intensity focused ultrasound (HIFU), radiofrequency ablation, laser ablation, and tissue freezing technique referred to as cryoablation [9-14]

High-intensity focused ultrasound (HIFU) is a type of noninvasive, local ablation therapy in which external ultrasonic energy is transmitted into a lesion using an extracorporeal approach, leading to coagulative necrosis of the tumor. Hence, targeted lesions are completely destroyed, leaving the skin intact [15]. HIFU technology was first described by Lynn et al in 1942. HIFU therapy has been used to ablate localized solid tumors. In the United States and European countries, MRI-guided HIFU is used mainly to treat prostate cancer and uterine fibroids, whereas in China, US-guided HIFU therapy is used to treat hepatocellular carcinoma and other solid tumors [16]. Among the other non-invasive treatment HIFU is an ideal breast-conserving therapy because HIFU does not significantly change the patient's mammary shape and does not cause bleeding or scarring after the procedure. Moreover, HIFU can preserve the structure and function of the breast postoperatively with outstanding cosmetic results. HIFU therapy can also maintain skin integrity and may play an important role in breast-conserving cancer therapies in the future. This article reviews the concept of HIFU, its application, and its advantages in the treatment of breast diseases.

2. Methods:

A comprehensive review of studies using non invasive ablative techniques; High-intensity focused ultrasound for the treatment of Breast fibroadenoma.

3. Principle of High-intensity focusedultrasound

The High-intensity Focused Ultrasound (HIFU) is a novel, extracorporeal non invasive image-guided device for the treatment of benign / malignant solid and soft tumors. Safety and feasibility have been studied extensively. HIFU is a completely non invasive ablative technique (Fig. 1) [16].

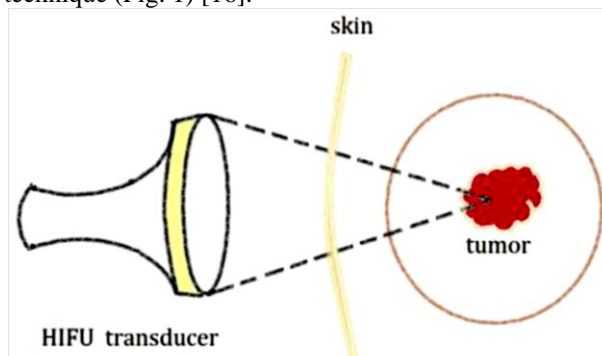


Fig.1: Diagram for the principle of High Intensity Focused Ultrasound (HIFU) for tumor treatment [17].

The use of therapeutic ultrasound for cancer

treatment was established by the 1970s [18]. Focused ultrasound surgery (FUS) is a noninvasive technique. By using the combination of high-intensity focused ultrasound (HIFU) and imaging method, FUS has the potential to ablate tumor lesions precisely. Recent advances in HIFU have increased its popularity. HIFU is used to manage a variety of tumors and palliative care [19, 20]. Ultrasound beams are generated by a piezoelectric ultrasound transducer and propagate through tissue as a high-frequency pressure wave. By focusing the ultrasound beams to a focal spot at a certain distance from its source, acoustic energy is converted to heat, and a sharp circumscribed lesion caused by thermal coagulation will be produced [21].

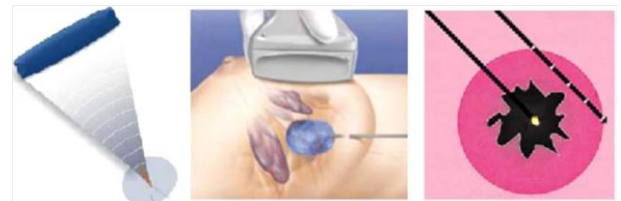


Fig. 2 Treatment overviews: (left) high-intensity focused ultrasound, (middle) cryo-ablation and (right) laser ablation (18, 19, 20)

The main mechanisms of HIFU ablation involve mechanical and thermal effects. The temperature reached within the focal point during a single sonication should be between 60 and 95°C. The mechanism for cell damage is primarily thermal [22]. Rapid increase in tissue temperature above 56°C for 1 s results in immediate protein denaturation and coagulative necrosis. The extent of cellular damage is determined both by the end temperature achieved and length of time for which it is maintained [23]. The skin and tissue surrounding the tissue lesion will be unaffected or show negligible temperature rise. The induced tissue lesion has a typical elliptical shape and a volume of 50–300 mm. For FUS ablation, ultrasound beams with frequencies in the range of 0.5 to 4 MHz are used depending on the application type and penetration depth that is to be attained, i.e., typical penetration depth is 20 cm at 1.5 MHz. The temperature reached within the focal point during a single sonication should be between 60 and 95°C. Rapid increase in tissue temperature above 56°C for 1 s results in immediate protein denaturation and coagulative necrosis [23].

4. Other non-invasive technology for the treatment of Breast fibroadenoma

Although the breast fibroadenoma is a common benign breast tumor, the treatment and follow-up of these lesions is still debatable. The management of fibroadenomas is still debatable and dependent on patient age and clinical findings. Surgical removal of tumor is one of the oldest and most established techniques for treating breast fibroadenoma. However, this technique has been largely replaced by newer modalities including Laser ablation, cryoablation, high-intensity–focused ultrasound ablation.

4.1 Laser ablation

Percutaneous laser ablation is a hyperthermia-based technique that destroys targeted tissues by using heat energy converted from absorbed light. Laser light is transmitted to the lesion via bare-tip quartz fibers with diameter of 300 to 600 μm inserted through multiple small-caliber needles (21 gauges). Inside the tissue, laser light travels for a short distance (12–15 mm) as a result of scattering, reflection, and absorption [24].

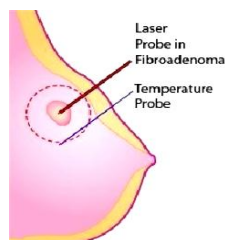


Fig. 3 Laser ablation of breast fibroadenoma [25]

The level of necrosis is dependent on the temperature and the ablation time. Laser ablation can induce very precise necrosis. The size and shape of thermal lesions are difficult to predict, however owing to biologic variability, fibre tip charring and changing optical and thermal properties of the tissue during interstitial laser photocoagulation

4.2 Cryoablation

The cryoablation procedure for breast fibroadenoma is relatively simple. After the lesion is localized under ultrasound guidance, a cryoprobe is introduced into the breast and guided into the center of the lesion, and cross-sectional diameters are measured. Cryoablation is based on the rapid cooling of the cryoprobe by the Joule–Thompson effect [26].

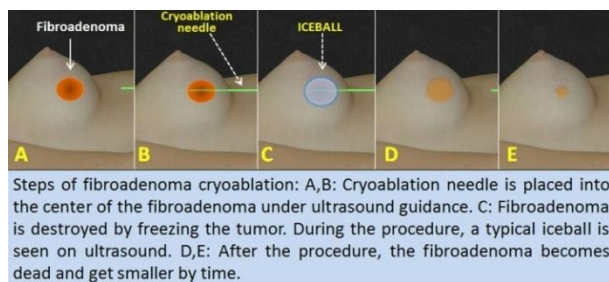


Fig. 4 Cryoablation of breast fibroadenoma [27]

Cryoprobe visualized in the center of the lesion. Real-time ultrasound is used simultaneously to guide the ice-ball formation. A double freeze-thaw cycle is always used. The forming ice-ball edge is highly echogenic, allowing for precise monitoring under ultrasound. Dripped and injected sterile saline between the skin and forming ice-ball that increases their distance from each other are available for skin protection. At the end of the procedure, the system should actively warm the cryoprobe to facilitate its prompt removal from the patients. Cell death is caused by direct intracellular ice crystal formation, resulting in physical damage to the

plasma and cytoplasmic organelle membranes [28].

4.3 High-Intensity–Focused Ultrasound Ablation

A multi-center clinical study to treat breast fibroadenomas with high intensity focused ultrasound (HIFU) has been launched in this Year and is currently recruiting 100 patients in the United States. The principal investigator of this single-arm prospective study is David Brenin, MD, associate professor of surgery and chief of breast surgery at the University of Virginia (UVA) Medical Center in Charlottesville. Additional participating centers include three New York City hospitals: Bellevue Hospital Center, Montefiore Medical Center, and New York in the Bronx, New York-Presbyterian/Columbia University Medical Center. High-intensity–focused ultrasound ablation (HIFU) is one of the thermal ablation therapies using high temperature to treat a targeted lesion. It is a noninvasive therapeutic modality, in which focused acoustic energy is precisely delivered from an extracorporeal source to the focal zone. This high-intensity–focused energy is then converted to heat, which destroys diseased tissues without damaging overlying and surrounding normal structures[28]. As the beam approaches the focal point, the power density of the converging ultrasound increases and the energy is accumulated at the focal zone. This phenomenon subsequently induces coagulation necrosis of the targeted lesion by creating acoustic cavitations and elevating tissue temperature to above 60°C . Temperatures can rise from 65 to 85°C ; however, higher temperatures are avoided to prevent boiling of liquids inside the tissue [23]. HIFU technology was first introduction in 1942, the technology of HIFU has continuously evolved, and recent developments have allowed its application to treat tumors of various solid organs, including the pancreas, liver, prostate, breast, uterus, bone, and soft tissue [24]. The effect of HIFU treatment was evaluated according to the changes in FA volume and improvement in clinical symptoms, including size by palpation and cosmetic concerns compared to baseline.

Kovatcheva et al had performed a multicenter study to assess the clinical outcome and safety of ultrasound (US)-guided high-intensity focused ultrasound (HIFU) in patients with breast fibroadenoma. In this study, they have described the first follow-up of US-guided HIFU ablation of breast FA with significant volume reduction at 6 and 12 months after the treatment (Fig. 5) [29]. From May 2011 to February 2013, 42 women with 51 FA in one or both breasts were selected for treatment with US-guided HIFU. Patients' age ranged from 16 to 52 years (mean 32 years). [29]

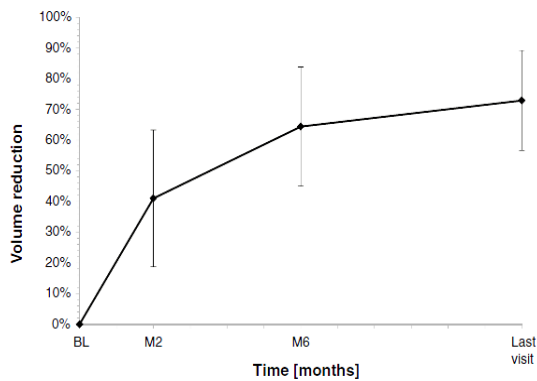


Fig. 5 Percentage of fibroadenoma volume reduction during the follow-up of US-guided HIFU treatment [29]

5. Management of fibroadenoma in developed country

Fibroadenomas are the most common benign breast masses in young women in world wide. In developed countries there are many techniques for the treatment of fibroadenomas, including; (I) conservative management, because that complete regression of one third of fibroadenomas will occur within 5 years. (II) surgical excision is the definitive therapeutic modality, but it has certain disadvantages which include the usual scheduling delays with the procedure; some cases have postoperative complications and incisional scarring, which compromises skin cosmetics and the anatomic contour of the breast; (III) ultrasound-guided vacuum-assisted fibroadenoma aspiration is a minimally invasive alternative, but its downside is that complete excision of the tumor is difficult to achieve. Several studies have demonstrated that the percutaneous cryoablation under ultrasound guidance is a safe and effective modality, and should be used as a primary alternative to surgical excision for breast fibroadenoma. Last few years more modern technology was trying to manage Breast fibroadenoma. Now a day's Focused ultrasound is the treatment of choice.[10.11]. HIFU is a technology using ultrasound waves to destroy cancerous tissue found in the breast. Kovatcheva et al demonstrated that US-guided HIFU treatment is an effective noninvasive method for the treatment of breast FA and well tolerated by the patients. Preliminary results are encouraging and show that HIFU could be an alternative to surgery for breast FA. Age-based algorithms that allow for conservative management and that limit excision to patients whose fibroadenomas fail to regress are presented

6. Management of fibroadenoma in Bangladesh

In Bangladesh, the preferred management of fibroadenoma is complete excision. However, this approach can lead to undesirable scarring or to extensive ductal damage if all the fibroadenomas are excised through one incision. Due to lack of awareness most of the patient in Bangladesh notices their breast problem in later stage.

7. DISCUSSION

Among the accumulated knowledge and information

about the treatment of breast fibroadenoma, non invasive treatment becomes more popular. Hynynen et al. were the first to describe the results of magnetic resonance (MR)-guided HIFU treatment of breast FA, which was successful in 73% of the cases [17]. They concluded that the treatment was both feasible and safe without marked adverse events. Recent advances in HIFU have increased its popularity. Some Promising results were achieved in managing various malignancies, including pancreas, prostate, liver, kidney, breast and bone.

8. CONCLUSION

In Bangladesh about two million women are affected by 2nd most occurring deathful breast cancer due to ignorance and their family member's unconsciousness and poverty. Most of the Bangladeshi women are uneducated and feel shy with society or husband to go doctor for checking breast problems. Early detection and diagnosis of breast tumor is imperative for improving patient survival. Now a day's medical technology of Bangladesh is gradually improving. Our review study in this paper introduces a new technique: High-intensity focused ultrasound for the treatment of breast tumor in Bangladesh that is easy, secure, time savable as well as cost effective.

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