SHORT REPORT

HIFU treatment for fibroadenoma — a clinical study at National Scientific Research Centre, Astana, Kazakhstan

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Abstract

This randomized controlled study evaluated effect of low frequency high intensity focused ultrasound (HIFU) in 80 women with breast fibroadenomas randomly and evenly divided into main and control groups, treated with HIFU and sectoral resection accordingly. In-vitro trial of fibroadenoma samples exposed to different power levels:100 Watt (W), 200 W and 300 W, analysis of results shown that optimal ablation power 200W was enough for coagulation necrosis of tumour, while 300W ablation caused complete destruction of tissues. Results showed that 20% of control group (surgically treated) patients had post-operative complications and 12.5% — postponed recurrences, as opposed to zero incidence of either in the main group (HIFU treated). The average hospital stay following HIFU reduced by 52%. Both in-vitro and morphological studies showed that HIFU caused high precision coagulation necrosis of fibroadenoma and preservation of the surrounding tissues. HIFU enabled to avoid early postoperative complications and long-term recurrences. This technique can significantly improve quality of life by reducing pain intensity and enabling sooner activity.

Keywords: High-intensity focused ultrasound (HIFU), HIFU treatment, Benign breast tumours, Breast fibroadenoma.

Introduction

The rate of benign breast diseases in women of childbearing age can reach as high as 30-70%; some proliferative form, accompanied by epithelial hyperplasia, considered as markers of increased risk for breast cancer.[1-3] Fibroadenoma is one of the most frequent diseases of the mammary glands and the major part of all benign tumours.[6-8] There is an increasing number of researchs on the development and introduction of new non-invasive treatment of breast fibroadenoma, some of which show great effectiveness of HIFU ablation in treatment of soft tissue tumours.

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This short report is based on the evaluation of the effectiveness of high intensity focused low frequency ultrasound in treatment of breast fibroadenoma in 80 women of reproductive age.

Patients/Methods and Results

The study involved 80 women with breast fibroadenoma treated at National Medical Science Centre in Astana over the period between 2013 and 2016. Breast fibroadenoma was clinically diagnosed by palpation, ultrasound diagnostics, MRI-imaging, cytology, aspiration and core biopsy, electron microscopy. They were evenly and randomly divided into the main group treated by HIFU method and control group who underwent traditional surgical technique (partial resection). Informed consents were signed by all patients. The following selection were applied: growth of fibroadenoma more than 1.5 times over a 1-2 year period,failure to treat conservatively for 2-3 years or more and age between 18 and 60 years. Mean age in both the main and control group was 30,00±1,745 and 35,00 ± 2,0455 respectively. Average fibroadenoma size in main and in control groups was 2,02×2,40cm^2 and 1,98×2,41cm^2 accordingly. Both groups were statistically relevant in terms of age and size of fibroadenomas.

All 80 patients previously received conservative therapy,i.e. drug treatment (hormone therapy), and were followed up by mammalogists at the place of residence.

Morphological studies (cytology, aspiration and core biopsy, electron microscopy), breast sonography and mammography were employed to evaluate the pre- and post-treatment data of main and control groups. SF-36 questionnaire was used to assess the patient's quality of life after treatment.

Experimental study in vitro was carried out during this investigation. We used four circular cross-sectional samples of fibroadenoma placed in pre-labeled plastic containers.

Sample 1 was not affected by HIFU and was used as a reference (control). Samples 2, 3 and 4 were ablated for 10 seconds with 100, 200 and 300W HIFU correspondingly.

Test material after the experiment was subject to

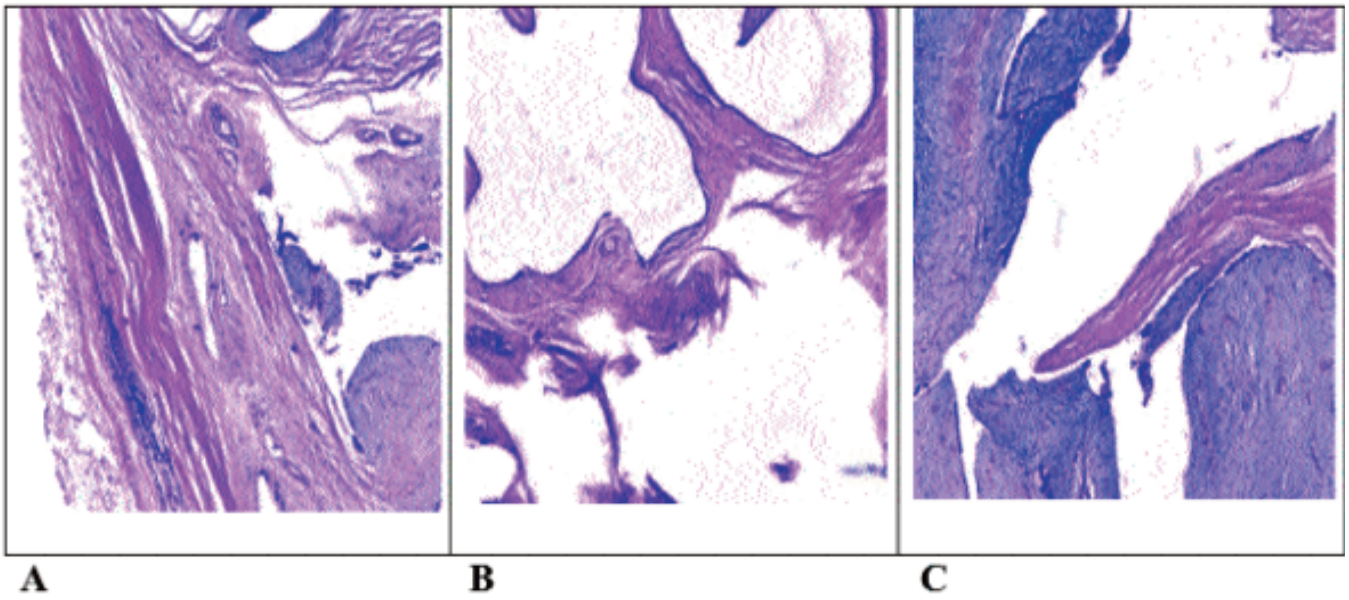

Table-1: Sample 3 (200 W).(A) Haematoxylin and eosin, x40. After tumour tissue ablation with 200W HIFU for 10 sec, largeexfoliative damage of stromal tumour component was observed. (B) Haematoxylin and eosin, x40.In areas of pericanalicular fibroadenoma, glandular structures are represented by cyst-type cavities. In areas ofintracanalicular fibroadenomas significant destruction was noted. (C) Haematoxylin and eosin, x40.Significant degradation of both glandular and stromal tumour component. Significant damageis seen at the tumour peripheral area.

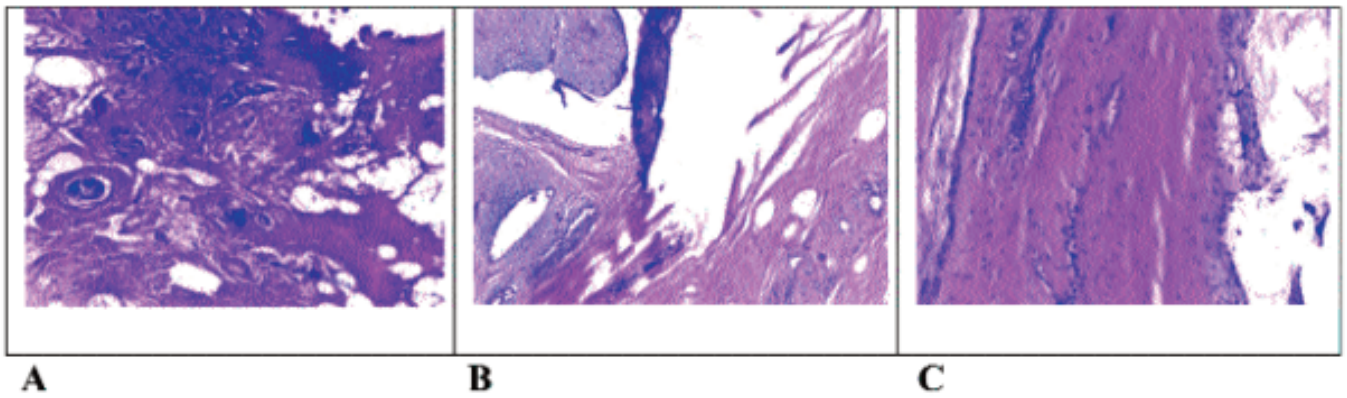

Table-2: Sample 3 (300 W). (A) Haematoxylin and eosin, x40.Extensive area of connective tissue without glandular component. (B) Haematoxylin and eosin, x40.Destructive zones of connective tissue are represented by small "perished" glandular structures. (C) Haematoxylin and eosin, x100.Significant exfoliationof stromal componentof intracanalicular fibroadenoma is observed.

morphology and cytologyassay.

To evaluate post-treatment quality of life in patients of both groups we used SF-36 questionnaire, in particular its scales "Pain Intensity" and "Physical Activity".

Standard traditional treatment for breast fibroadenoma remains sectoral resection.

HIFU ablation of fibroadenomas was performed with 21.5 cm therapeutic lens, 1MHz frequency and 16.2 cmfocal length.

Effectiveness of HIFU-therapy was assessed by the comparative analysis of complications rates, recurrences, and length of hospital admission. Quality of life was assessed by SF-36 questionnaire.

Results of morphological studies in vitro.

The morphology study showed the stepwise dependancy of tissue changes correlating to the ablation power. Ablation with 100W HIFU caused initial coagulation changes in tissues. Next step of 200 W HIFU applied to the tumour caused advanced coagulation necrosis. Hence,

200W dosage can be recommended as sufficient power for optimalablation, whereas 300W dosage causes complete destruction of tissue.

No intra-or postoperative complications related to HIFU-therapy were recorded in the main group. Eight patients in the control group (20%) had early post-operative complications: in the form of infiltration (5), haematoma (2) and abscessis (1).

Patients of both groups were under our post-treatment monitoring for two years. No recurrences were registered in the main group during that period whereas relapses occurred in 5 (12.5%) patients of the control group, which presented as single fibroadenoma at the site of the surgical intervention. In 3 patients these were diagnosed at the third monitoring visit, i.e. 12 months after the surgery, and in 2 patients — after 18 months. The sizes of reoccurred fibroadenomas were 7 to 11mm.

With regards to hospitalization length, there was a statistically significant difference between main and control groups ($p < 0.05$). Admission length for HIFU-treated patients was 3.9 days in average, while for the control group it accounted for 7.4 days, showing a 52% decline in hospital stay for HIFU-treated group.

According to the results of SF-36 questionnarie,the level of pain was 66.7% higher in the control group. On the other hand, physical activity amongst HIFU patients was 44.7% greaterthan that of the control group. Both indicators presumed better quality of life after HIFU treatment compared to the surgical resection.

Conclusion

1. Results of both in-vitro andmorphological studies showed HIFU-induced coagulation necrosis and following fibrosis of fibroadenoma tissue. This technique allows high-precision removal of fibroadenoma and preservation of the surrounding healthy tissues without deformation of breast contours.

2. HIFU enables to avoid early postoperative complications and long-term recurrences in women of childbearing age with breast fibroadenoma.

3. HIFU can improve quality of life compared with surgical treatment, reducing intensity of pain by 44.7%, allowing earlier return to active functioning by 66.7% and reducing length of hospital stay by 52%.

4. Being a new non-invasive technique of breast fibroadenoma treament for women of childbearing age, high-intensity focused ultrasound — is a promising trend in practical medicine.

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