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Application of New Ultrasound Technology in Spinal Cord Injury: A Systematic Review

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Introduction: High Intensity Focused Ultrasound is non-invasive technique therefore, there is no need for surgery or ultrasound-guided puncture and no risk of bleeding. It can completely destroy lesions in the body, with no harm to ultrasound-penetrated tissues or normal areas lying outside the target. This review aiming at highlighting use of HIFU in spinal cord surgery.

Methods: The electronic search resulted in ten potentially relevant studies that reported to assess Outcomes of High Intensity Focused Ultrasound in different surgical procedures. Eight studies were excluded because of that they were not consistent outcome.

Results: All the included studies were prospective studies except only one was retrospective study which was done among 73 patients aged between 17-80 years with benign thyroid nodules. The treatment was done using an image transducer and HIFU transducer. The outcome of HIFU was varying among different surgical and spinal cord procedures. Five of included studies were measuring the survival rate, it was ranged between 38.5% and 89%.

Conclusions: The HIFU is a promising non-invasive technology that can enhance neurological surgery with faster recovery and less post-operative complications.

Keywords: Spinal cord, Surgery, Ultrasound, High intensity

Introduction

High-intensity focused ultrasound (HIFU) is a technology that permits the use of ultrasound waves used for imaging and then focuses them as one would use a magnifying glass to focus sunlight. The ultrasound energy is absorbed by tissue and converted to heat and can be used to ablate tissue [1]. In addition, a type of nonsurgical therapy, previous research has suggested that high-intensity focused ultrasound (HIFU) is a safe and effective method for uterine fibroid [2], pancreatic cancer [3] and liver cancer [4].

In animal experiments and clinical studies, HIFU can selectively target and destroy primary or metastatic lesions by skin absorption, thereby treating tumors in several organs [5]. HIFU was used for treating various lesions, and it could be an effective alternative minimally invasive therapy for the achievement of local control of intra-abdominal aggressive fibromatosis [6] and it was found that HIFU recovery is faster and less expensive [6] Moreover, HIFU treatment is a noninvasive technique that can induce complete coagulation of the tumor necrosis target without surgical exposure or insertion of instruments into lesions. The main objective of HIFU is to provide high response rates for traditional therapies with few side effects [7]. HIFU safely and noninvasively ablated malignant bone tumors and relieved pain. HIFU ablation should be further investigated, as it appears to be successful in the treatment of primary malignant bone tumors [8] it is also a noninvasive method for the treatment of localized tumors [9] and could be an effective alternative modality in the treatment of symptomatic adenomyosis [10]. HIFU is a potentially effective treatment of localized pancreatic cancer, with low mortality rate [11].

It is a safe and effective therapeutic option for patients with advanced prostate cancer. This treatment can be effective for local tumor control [12]. HIFU safely and noninvasively ablated malignant bone tumors and relieved pain. HIFU ablation should be further investigated, as it appears to be successful in the treatment of primary malignant bone tumors [8]. HIFU is non-invasive US technique therefore, there is no need for surgery or ultrasound-guided puncture and no risk of bleeding. HIFU can completely destroy lesions in the body, with no harm to ultrasound-penetrated tissues or normal areas lying outside the target. Secondly, there is uniform distribution of therapeutic dose. Non-uniform dose distribution is a problem in minimally invasive, interventional therapies like microwave, radiofrequency, laser, and freezing. Another advantage is that lethal treatment of the targeted area is possible.

The target receives lethal ultrasonic doses and all tissues within the target are non-selectively destroyed [13]. HIFU is a type of conformal treatment; 3-dimensional conformal therapy ensures complete lesions that are unconstrained by tumor shape. HIFU treatment is not dependent on tumor size; lesions of any size can be completely destroyed. It also allows selective destruction of blood vessels [13]. Real-time treatment is possible; ultrasound monitoring devices offer real-time monitoring of the entire process of HIFU treatment, enabling timely evaluation of treatment efficacy and dose adjustments using imaging changes of the target before, during, and after treatment [13]. This review aiming at highlighting use of HIFU in spinal cord surgery. The key to HIFU treatment is that the energy delivered is sufficient to increase the tissue temperature to a cytotoxic level very quickly so that the tissue vasculature does not affect the extent of cell killing. Heat coagulation by HIFU is desired for cell reaction with chronic inflammation, and histological signs of fat necrosis in the surrounding normal fatty tissue [9]. Large blood vessels seem less vulnerable to HIFU damage compared to tumor tissues.

This is likely due to dissipation of the thermal energy from the vessel wall by the blood flow, which results in safe ablation of the tumor. Deadly complications may also develop if any vital blood vessels are damaged during ablation. This is important when surgical resection of a tumor is contraindicated and ultrasound ablation may be dangerous because of close proximity to major vessels.

Methods

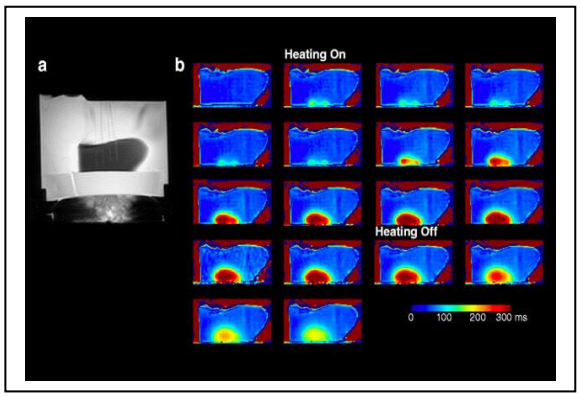
The electronic search resulted in ten potentially relevant studies that reported to assess Outcomes of High Intensity Focused Ultrasound in different surgical procedures. Eight studies were excluded because of that they were not consistent outcome. The protocol of this systematic review was written in accordance with the PRISMA-P (Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols) guidance.

An online literature research was conducted using PubMed access. The algorithm used the terms: “CEUS” “contrast-enhanced ultra-sound” “brain” “neurosurgery” “hydrocephalus” “aneurysms” “brain perfusion” “stroke” “carotid plaques” “glioblastoma” “brain tumors” “AVM” “cerebral aneurysms” as key words in various combinations. Many unique articles were identified. After the searches, the duplicates were removed (n = 10). The abstracts found in multiple searches to identify potentially eligible articles for inclusion were read. The following criteria have been used to identify studies to be included in the review.

Studies involving humans treated for a neurosurgical condition were considered for inclusion. Any study evaluating CEUS application in a clinical neurosurgical setting were retained for inclusion in the review. We included any study matching the aforementioned criteria and reporting original data. Since the paper aims in highlighting unconventional CEUS uses, were included in the review.

Results

The search resulted in ten potentially relevant studies that reported to assess Outcomes of High Intensity Focused Ultrasound in different surgical procedures. Eight studies were excluded because of that they were not consistent outcome. Overall sample size was ranged between 15 [18] and 1002 [15]. The minimum age was 9 [18] years old, while the maximum was more than 18 years old [10]. All the included studies were prospective studies except only one was retrospective [16] which was done on 73 patients aged between 17-80 years with benign thyroid larger nodules. The treatment was done using an image transducer (7.5MHz, 128 elements, linear array) and HIFU transducer (3 MHz, single element, 60mm in diameter). After positioning, patients were sedated with diazepam (10–15mg) and pethidine (50–100mg). Under USG guidance, the treatment head was adjusted until the entire index nodule was within the treatable depth. The outcome of High Intensity Focused Ultrasound was varying among different surgical and spinal cord procedures. Five of included studies were measuring the survival rate, it was ranged between 38.5% [8] and 89% [11].



The lowest survival rate was seen in a prospective study done by (Li, C., et al. 2010), it was done on 25 patients with mean age of 39.6 years old, the surgery was performed for ablation of malignant bone tumors. (Model JC, Chongqing Haifu Technology, Chongqing, China) used in this study was guided by real-time ultrasonographic imaging. The five years survival rate was 38.5%, for patients with primary bone tumors [8]. While the highest survival rate was seen in a prospective study done by Crouzet, on 803 patients with mean age of 70.8. The surgery was done for ablation of localized Prostate Cancer. HIFU propagates ultrasound waves generated by a spherical transducer placed in the rectum. HIFU works by focusing high-power acoustic waves on a specific focal point to produce temperatures of 85 °C [6. These temperatures are high enough to cause cellular disruption and coagulative necrosis at the focal point of the HIFU acoustic waves. The overall survival rate

at 8 years was 89% [11]. Two of included studies measured the volume reduction, the first study was done on the thyroid with overall median 6-month volume reduction of 68.3% [16]. while the second study was a prospective study, it was done on 17 patients, with mean age of 67 years old, the surgery was done for ablation of renal cell carcinoma (RCC). Model-JC System (Chongqing HAIFU, China), under general anesthesia with one overnight hospital stay. Real-time diagnostic ultrasonography was used for targeting and monitoring. patients were evaluated at the 6-month follow-up; eight tumors had involuted, mean 12% decrease in tumor area [17]. A prospective study done by Gelet calculated the disease-free rate on patients, with mean age of 71 years old. The surgery was done for ablation on of prostate cancer, the treatment parameters (3.0 MHz nominal frequency, 5.0-second treatment pulse, 5.0-second shot interval) were selected to optimize the size of the lesion while leaving rectal wall and surrounding tissues intact. Complete success and clinical effectiveness were calculated in two of included studies. The first study was a prospective non-comparative interventional clinical study, it was done on 30 patients, with mean age of 62.9 years, ranging between [21–87] years. The surgery was open-angle glaucoma.

The visual field was examined using an automated diagnostic system (Humphrey Field Analyzer; 24-2 SITA-standard program; Carl Zeiss Meditec, Dublin, CA, USA), UBM with a 50-MHz probe (Aviso; Quantel Medical, Clermont-Ferrand, France) and OCT with a Cirrus OCT (Carl Zeiss Meditec). For UBM, radial and transverse scans were obtained at 0°, 45°, 90°, 135°, 180°, 225°, 270° and 315° meridians. Complete success was seen in 46.7% of eyes [14]. While Clinical effectiveness was measured in a study done on Seventy-eight patients aged more than 18 years old. High-intensity focused US ablation was done for treatment of adenomyosis, it was performed with use of the Haifu JC Focused Ultrasound Tumor Therapeutic System (Chongqing Haifu Tech Co., Ltd., Chongqing, People's Republic of China). Each patient received one session of HIFU ablation as an outpatient. The treatment was performed outside of menstruation. Before treatment, patients underwent careful bowel preparation and were asked to shave the hair of the anterior abdominal region from the umbilicus to the upper margin of the pubic symphysis. During the procedure, a urinary catheter was inserted into the bladder and filled with degassed sterile water through an infusion set to control the bladder volume. Intravenous conscious sedation (fentanyl and benzodiazepine) was administered. The clinical effectiveness was (89.9%) [10].

Discussion

High-intensity focused ultrasound (HIFU) is a nonsurgical therapy [15]. The lowest survival rate in this review was seen in a study done by Li et al., among 25 patients, HIFU was performed for ablation of malignant bone tumors [8]. The five years survival rate was 38.5%, the small sample size may limit the outcome. Tumor reduction volume was calculated in a study done in ablation of renal cell carcinoma with mean 12% decrease in tumor area [17]. This could be related to that device does not generally allow complete ablation in a large area in diameter because of the mechanical limits of the device [16]. High-intensity focused US ablation was done for treatment of adenomyosis, the clinical effectiveness of it was 89.9% [10].

The results of this study show that US-guided HIFU ablation appears to be a safe intervention for the treatment of adenomyosis. In addition, this method is well tolerated by patients [10], Currently, US-guided HIFU ablation represents an important development in this field [10]. A prospective study done by Gelet calculated the disease-free rate of prostate cancer and it was 68% [19]. The cancer control effectiveness of any treatment approach for prostatic cancer is influenced by three factors: efficacy as primary therapy, early detection of relapse, and feasibility and efficacy of curative salvage options [15]. One of the advantages of HIFU is that it can be repeated in the case of recurrence or to re-treat a prostatic site, it involves no radiation, and patients do not suffer from long-term irritative urinary symptoms [20].A retrospective study which was done on patients with benign thyroid nodules with a volume reduction of 68.3%, Single-session HIFU ablation was highly effective in causing shrinkage of benign thyroid

nodules but the extent of shrinkage for larger-sized nodules was noticeably less than that of smaller sized nodules. additional HIFU treatment after initial treatment might be preferred over sequential treatment within the same session [16].

Both thermal and non-thermal (cavitation) effects play a very important role in all therapeutic applications of ultrasound. The side effects of these two mechanisms of action can be injurious biologically and are therefore avoided in diagnostic applications of ultrasound but can be beneficial in therapeutic applications. The ability to focus the ultrasound beam to a small area a couple of millimeters in size enhances both the thermal and non-thermal effects of ultrasound and results in ablation and necrosis of cells at the applied focal point [17]. This makes ultrasound an excellent non-invasive therapeutic ablation technique for deep-seated targets within the body. HIFU therapy provides a less invasive approach to cancer therapy that minimizes discomfort to the patient and length of hospital stay. Initial studies have demonstrated HIFU to be generally safe and clinically effective and to have high potential clinical acceptance. However, HIFU is still in its infancy and further studies are necessary (especially in the field of oncology and the brain) regarding the long-term medical benefits, technical considerations, and treatment delivery before transition to more widespread use [19].

Conclusion

The HIFU is a promising non-invasive technology that can enhance neurological surgery with faster recovery and less post-operative complications. The range of HIFU applications may expand in the future with improved imaging. MRgFUS is one of the most successful imaging guide approaches. However, there is a need for additional studies with longer-term follow-up.

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