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# A review of high-intensity focused ultrasound as a novel and non-invasive interventional radiology technique

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ABSTRACT

High-intensity focused ultrasound (HIFU) is a non-invasive interventional radiology technology, which has been generally accepted in clinical practice for the treatment of benign and malignant tumors. HIFU can cause targeted tissue coagulative necrosis and protein denaturation by thermal or non-thermal effects, guided by diagnostic ultrasound or magnetic resonance imaging, without destruction of the normal adjacent tissue, under sedation or general anesthesia. HIFU has become an important alternative to standard treatments of solid tumors, including surgery, radiation, and medications. The aim of this review is to describe the development, principle, devices, and clinical applications of HIFU.

## 1. History and advantage of high-intensity focused ultrasound (HIFU)

Interventional radiology (IR) is a minimally invasive technique guided by imaging devices, such as magnetic resonance imaging (MRI), computed tomography (CT), ultrasound, and digital subtraction angiography. As part of IR,[1] HIFU interventions include MRI or diagnostic ultrasound to accurately target tumors and monitor surgeries. The main advantage of HIFU over conventional interventional radiological techniques is its non-invasive nature and the absence of X-ray exposure. As a long-standing clinical interventional technology, HIFU has been utilized for 80 years. Dating back to history, in 1935, Grutz found that short ultrasonic waves could be focused by covering a concave curvature on the surface of a vibrating quartz plate. Lynn proposed the definition of high-intensity focused beams in 1942. John created a focused ultrasound generator and used ultrasound in therapy through local heating control in the 1940s. Burov proposed using HIFU to treat patients with melanoma tumors in the 1950s. Ballantine was the first to use therapeutic focused ultrasound (FUS) to treat psychiatric disorders, such as Parkinson's disease, in 1960.[2] However, these early efforts were unsuccessful due to the lack of a suitable acoustic window because of the skull shield and the poor convergence quality of the ultrasound. HIFU has been clinically accepted mainly for the treatment of glaucoma by decreasing intraocular pressure. Until 1962, William Fry utilized FUS to treat Parkinson's disease, and 50% of patients had their symptoms resolved. Lower-intensity ultrasound was used for tumor treatment in the 1970s.[3] Gelet ablated prostate cancer using HIFU in 1992 and published the result in 1996.[4]

## 2. Mechanism and device of HIFU

The frequency of diagnostic ultrasound is 1–20 MHz, which is generated by piezoelectric particles that can convert electric signals into sound waves. However, the frequency of HIFU is 0.2–4 MHz, which is produced from a generator with a maximal compression pressure of 20–70 MPa and intensity of 100 to 10, 000 $W/cm^2$.[5] HIFU devices consist of a generator that can produce ultrasound energy and a transducer that focuses the ultrasound energy produced by the generator on a target lesion. The transducer contains many particles that can modulate ultrasound in amplitude and frequency.[6] Non-linear wave transmission, mechanical action, heat effect, and cavitation of ultrasound play an important role in HIFU.[7] The main mechanism of HIFU is the conversion of ultrasound mechanical energy into cavitation and heat energies. Then, this ultrasound is focused on the targeted tissue similar to a magnifying glass concentrating the sun's rays to a point which has the highest temperature. The temperature of the focus can increase rapidly above 80 °C at once,[8] causing targeted volume coagulation necrosis with no destruction to the surrounding tissue, and the focused lesion tissue damage shows a high echo during ultrasound.[9] When ultrasound passes through the soft tissue and remains in the target tissue, it is called an

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absorption coefficient. Concurrently, other sound energy is reflected in all directions causing an acoustic energy loss by the surrounding tissue, which is called the attenuation coefficient. Different tissues have different ultrasound attenuation coefficients, ultrasound frequencies, and total emitted ultrasound energy. In total, the optimal treatment energy and effective adsorbed ultrasound energy are decided by the target tissue blood supply, ultrasound penetration depth, and hyperthermia rate, as well as ultrasound intensity and local tissue absorption coefficient. To ensure that the target tissue receives more energy, the reflection effect must be minimized and more heat deposition should be accomplished.[10] Another potential effect mechanism for tissue damage is acoustic cavitation attributed to the microbubbles in the target tissue forming a high acoustic intensity, which is dependent on the tissues causing a blast micro-shock wave phenomenon, damaging the target and surrounding tissues.[11] The application of cavitation is generally positive, and it is used in the treatment of benign and malignant tumors, as it may augment ablation volume and improve the effectiveness of the treatment; however, it also induces unpredictable side effects, such as damage to the surrounding tissues. For instance, SonoVue contrast induces an increased formation of gas bubbles to improve cavitation of the target tissue, which leads to more tissue necrosis. Simultaneously, the contrast allows the ablated region to become visible. As a result, the target tissue is ablated and undergoes coagulative necrosis by hyperthermia and non-thermal mechanisms. The extent of tissue necrosis is dependent on the achieved temperature and blood supply of the target tissue and the duration of ablation. The abundant blood supply in the target tissue makes the deposition of ultrasound energy much harder. Similarly, larger tissue volumes also require an increased amount of ultrasound energy to undergo thermal damage in the target region. The volume of ablation after HIFU is typically a small, oval, rugby ball-shaped lesion in the focus with a dimension of 2mm width and 13mm length along the ultrasound axis section. HIFU can converge high-power ultrasound with a wave length of 0.2–0.3 mm onto tissue with a volume of $9 \times 2 \times 2$ mm$^3$.[12] Histology reveals a sharp edge between live and dead cells. HIFU can provide an absolutely non-invasive treatment without causing destruction to the non-targeted tissues. Therefore, large tissue volumes with abundant blood supply require an increased amount of ultrasound energy to induce thermal damage in the targeted tissue. HIFU energy exposure quantity is adjusted until the total treatment volume achieves a hyperechoic region or the tumor has no contrast perfusion on the guiding ultrasound image, indicating that the target tissue has completely necrosed.[13]

## 3. US and MRI-guided HIFU

The monitoring equipment of HIFU includes an ultrasound (USgHIFU) system and a magnetic resonance imaging (MRgHIFU) device. Both these devices have shown efficacy in locating the target region and receiving timely feedback from the target region during treatment.[14] The guiding ultrasound allows the establishment of a treatment plan and monitoring of the region of treatment in real time. Diagnostic and therapeutic ultrasound transducers are used in the same device; however, the transducer is directly installed in the MRI system. The advantages of ultrasound guidance include ease of access, real-time visualization of the treated volume and energy deposition in the treated area, precise display of the target tissue, and detection of any movements by the patient during the treatment.[15] Skin changes during treatment can be monitored using ultrasound guidance. The effective use of ultrasound guidance is related to operator experience; however, the target tissue may be displayed with difficulty because of air or movement of the surrounding cavity organs.

Another advantage is that the SonoVue contrast agent can distinguish non-treated tissue and left tissue blood supply.[16] Another guidance with MRI HIFU system include workstation and console, control therapy station with a computer. The MRI device contains a US transducer which is set on a mechanical arm. The computer can communicate with the MRI device, so the operator can integrate the MRI procedure into the HIFU workstation, which allows ablation to be performed. It uses the MRI temperature map to locate the target lesion and the surrounding tissue anatomy to monitor the temperature and adjust the treatment in real time.[17] This positive feedback can adjust local tissue variations, which lead to heterogenous absorption and attenuation. It contains a thick membrane with 0–19 °C water to cool the skin, which is decided by personal experience during the treatment. The targeted tissue volume is verified by an MRI map.[18] MRI can provide accurate anatomical images because of its high resolution, high sensitivity for lesion detection, and timely display of the temperature of the targeted tissue, which is a well-defined small, focused point. Moreover, it also displays the necrosis tissue volume with a temperature higher than 56 °C, causing a precise and targeted ablation, which is quantitative thermometric temperature mapping.[19] The advantage of MRgHIFU is that it can provide accurate quantitative feedback from the target region and allow assessment of thermal exposure dose distribution on target tissues; thus, total energy power delivery and temperature measurements can be assessed; however, it is very expensive. The probe is classified as an in-body and out-body probe. In-body probes are inserted rectally. A transrectal HIFU has been applied for the treatment of prostate tumors and benign prostate hyperplasia with some encouraging results.[20] Both the therapy transducers take a hemispherical bowl form and focus the acoustic beam in a cone. In 2001, Prat described a probe installed for biliary tumors with intraductal treatment. The flexible rotational probe can be placed in a fluoroscopic guide for circumferential ablation. A $3 \times 10$ mm and 10-MHz complanate transducer that produces an ultrasound intensity of 2–14 W/cm$^2$ for 10–20 s bursts is positioned on a shaft. The transducer can rotate by 18° after each "click." Once a tissue has been damaged, the probe is located repeatedly under ultrasound guidance. Similarly, an MRI guiding intracavity device was used for esophageal tumor treatment in 2005. The disadvantage of an intracavity HIFU is the propensity for burns in the rectal and esophageal wall.[21]

## 4. Clinical applications of HIFU

The first clinical application of HIFU was for the management of kidney stones in the 1990s, until it was discovered that it could induce coagulative cell death of the focused areas in the tissue. Currently, HIFU is being used in the treatment of both benign and malignant solid tumors, such as uterine fibroid, uterine adenomyosis, scar pregnancy, osteoid osteoma, bone metastases, hepatocellular cancer, pancreatic cancer, mastocarcinoma, breast fibroadenoma, lymph node tumor, prostate carcinoma, and other solid soft tissue tumors.[22] HIFU can focus ultrasound onto a point to increase heat quickly to kill tumor cells. The advantages of HIFU in treating tumors include the following: non-invasiveness, safety, provision of pain relief, and improved efficiency of oncologic drug release to the tumor.[23]

(1) Liver cancer

Liver cancer is the fifth most common malignant solid tumor in the male population, usually occurring in patients with chronic hepatitis and cirrhosis, which accompanies liver dysfunction. Hepatic resection is the first choice for patients with hepatocellular carcinoma (HCC) less than 3-cm in diameter in many hospitals. For more advanced HCC, transcatheter arterial chemoembolization (TACE), radiofrequency ablation (RFA), and systemic chemotherapy are frequently offered as palliative therapies. HIFU is a promising therapeutic alternative for patients in whom surgery or mini-invasive therapies are not feasible. The thermal ablation phenomenon of HIFU has been used in patients for the management of primary and secondary liver tumors, especially primary HCC. Ji treated HCC using HIFU combined with TACE with promising clinical results. Nevertheless, cirrhosis and ascites that accompany HCC limit the usefulness of surgery and also increase the risk of liver failure after surgery. According to the level of liver function and the number, size, site, and blood supply of hepatic malignancies, several chemical, thermal, and electrical therapies can be used, such as ablative therapies, TACE, hepatic artery infusion chemotherapy (HAIC), targeted drug therapy, and immuno-drug therapy. Therefore, many different therapeutic methods should be used in combination. HIFU can not only cause cancer necrosis but also improve the efficacy of synergistic chemotherapies, such as TACE and HAIC, for the management of HCC. The deposited iodinated oil can increase the thermotherapy effect and the chemotherapy drug release time to cause cancer cell death. HIFU can lead to the release of chemotherapy agents, such as pirarubicin, oxaliplatin, and so on. Thereafter, the liver tumor becomes necrotic and smaller, delaying the spread. More importantly, some studies showed that patients with HCC treated with HIFU had an increased 5-year survival rate, overall survival (OS), and progression free survival (PFS).[24] Some studies showed that HIFU can restore hepatic metabolism, improve the quality of life, enhance immunity, and significantly reduce tumor markers such as AFP, CEA, and CA199. Concurrently, it has fewer adverse reactions, including jaundice, ascites, gastrointestinal reactions, and liver discomfort.[25]

(2) Kidney cancer

Most patients with renal cancers are asymptomatic. Renal cancers are usually diagnosed incidentally and account for 700,000 deaths every year worldwide. Currently, the standard treatment of renal tumors is surgical resection, including radical or partial nephrectomy which has many complications or can cause acute morbidity.[26] Simultaneously, some patients lose the chance of surgery or are unwilling to undergo surgery. RFA and cryoablation, in which the complication rate is low, have been applied predominantly in older patients. However, there is an increased possibility of hemorrhage, renal function injury, and tumor recurrence in RFA than in cryoablation.[27] HIFU is completely non-invasive and safe, with lesser side effects, and does not impair renal function. However, if the kidney tumor has an abundant arterial blood supply, the tumor arteries must be embolized before HIFU. Kidney artery embolization can cause a major part of tumor necrosis. HIFU can cause coagulative necrosis of the entire tumor.[28] A clinical study showed that HIFU treatment is feasible, safe, and curative, with lower morbidity in treating renal tumors without risk of hemorrhage, kidney dysfunction, and tumor spillage. Nearly 50% of kidney tumors become smaller in size, as observed on CT or MRI scans after HIFU treatment for 2 weeks. About 67% of patients with kidney tumors treated by HIFU achieved stable lesions after 2 years of treatment. The advantages of HIFU over surgery include its non-invasiveness, absence of X-ray exposure, easy tolerance, preservation of renal function, faster and effective recovery, fewer complications, and longer OS.

(3) Cesarean scar pregnancy

The prevalence of cesarean scar pregnancy (CSP) is increasing due to the three-child policy and augmentation of cesarean section; it is no longer a rare event, particularly in the mainland. Manifestations of CSP are abdominal pain and irregular vaginal bleeding. CSP will lead to infertility. In a study, women with CSP were treated with surgery, uterine artery embolization (UAE) with curettage, and HIFU with curettage. Therapeutic effect assessment included total blood loss, decline of hCG, pain relief rate, and duration of hospital stay. The cure rate of surgery, HIFU, and UAE was found to be 98%, 70%, and 44%, respectively. Furthermore, hCG declined rapidly in the surgery group, and HIFU was suitable for those CSP patients with a gestational age of $<$55 days and a sac diameter of $<$3 cm. HIFU can preserve the patient's fertility, and produce fewer complications and is safe.[29] Some studies show that HIFU and UAE have the same curative effect for CSP, but HIFU results in fewer adverse reactions and complications, shorter hospitalization time, lower cost, lesser bleeding, no hemorrhage during the process, and is non-invasive, accurate, and repeatable. HIFU is the best choice for CSP patients with a high hCG level, large gestational sac, and long gestational time, especially for patients with re-pregnancy at the scar site after cesarean section, which can increase the uterine retention rate.[30] HIFU is safe, effective, precise, requires no X-ray exposure, and causes less pain in the treatment of CSP patients. It can retain the functional integrity of the uterus.

(4) Pancreatic carcinoma

Pancreatic carcinoma is the most lethal cancer due to the absence of specific symptoms in earlier stages, and approximately 80% of patients lose their chance for surgery by the time the diagnosis is made.[31] Severe abdominal pain, loss of appetite, easy fatiguability, and impairment in physical and emotional function are major concerns during palliative care. Most of the cancer cells invade the superior mesenteric artery, celiac trunk, or portal vein. These terminal patients have limited benefits from recent treatment modalities and are affected by abdominal or back pain and depression due to the non-resection of the tumor. Gemcitabine, leucovorin, fluorouracil, irinotecan, and oxaliplatin are the various drugs used for chemotherapy for the management of pancreatic carcinoma. However, these drugs induce toxicity, and the survival outcome is not satisfactory. Other therapies include RFA, microwave ablation (MWA), and cryoablation; however, these methods are considered invasive. HIFU can effectively ablate pancreatic tumors, destroy tumor cells, and enhance the delivery of chemotherapy. Some studies show encouraging results in that HIFU combined with chemotherapy has desirable clinical efficacy.[32] HIFU treatment mainly relieves pain, which is beneficial because most patients with pancreatic cancer are in the late stage of the disease without the opportunity for pancreatic resection.[33] HIFU treatment can cause coagulative necrosis in pancreatic cancers without destroying the structure of the pancreas. HIFU mainly protects the integrity of the pancreas and has a lower rate of side effects. Complete tumor and margin necrosis have been shown by HIFU ablation in clinical trials.[34] HIFU is a promising treatment besides systemic palliative chemotherapy. Currently, all studies confirm that HIFU can significantly reduce patients' pain with less treatment-associated complications and lead to a 7–16-month OS in these patients. Pain relief is because of cancer necrosis and subsequent tumor shrinkage and because pain medication is more easily tolerated. HIFU can guarantee symptomatic pain relief and improved quality of life in all stages of pancreatic cancer. HIFU has become a promising and important complementary method for the management of this fatal disease.

(5) Prostate cancer (PC)

PC is one of the most frequent and rapidly increasing malignancies in the world[35]; 70% of PC cases are local and suitable for surgery and radiation.[36] However, these therapies have several complications and risks. Concurrently, surgery or radiation is not suitable in some older or weaker patients. HIFU can destroy deep tissues without any skin incision. HIFU has been assessed to be effective in localized PC treatment for patients who could not have benefited from surgery, who refused surgery, or for whom the tumor recurred after radiation.[37] Undoubtedly, HIFU has been well studied and utilized in clinical practice as a salvage therapy after a failed surgery and radiation treatment.[38] Adverse events of surgery and radiation include urinary tract stricture/stenosis, retention, infection, incontinence, potency, and pain. Transrectal HIFU ablation is a non-invasive treatment that can maintain a low prostate-specific antigen level and less tumor diameter in PC patients. HIFU uses real-time imaging guidance and can destroy targeted tissue by ultrasound thermal, cavitation, and mechanical effects without a skin incision, while preserving the surrounding tissues and organs. The HIFU process causes little pain and can be applied with conscious sedation.

As a curative treatment option, it is suitable, safe, and effective for non-resection patients with PC.

(6) Bone tumor and metastases

Some studies show that HIFU ablation in the musculoskeletal field is safe and feasible, such as for the management of bone metastasis, osteoid osteoma, desmoid tumor, and facet joint osteoarthritis in which HIFU can relieve pain and control tumor progress. MRgHIFU is the best treatment for benign, malignant, and metastatic bone tumors. The main aim of HIFU is to relieve pain palliatively and preserve the limbs. Rodrigues has analyzed the clinical effect of MRgHIFU for the management of bone tumors, and they found 96%, 86%, and 75% efficacy for the management of primary benign tumors, primary malignant tumors, and metastatic tumors, respectively.[39] In fact, HIFU induces targeted bone full ablation necrosis, which increases the risk of bone fracture and related nerve fiber injury. The operator should have a satisfactory knowledge of anatomy and a good knowledge of ultrasonic energy dose. MRgHIFU can generate temperatures above 55 °C, causing protein coagulative necrosis, protein denaturation, and cell destruction and can more distinctly show the region of interest on the image than that of USgHIFU. MRI shows real-time monitoring of temperature mapping, thus avoiding superfluous ultrasound energy from impairing the surrounding tissue. The advantages of HIFU over RFA, MWA, and radiation therapy, in which anesthesia and recovery durations are similar to that of HIFU, include its complete non-invasiveness and absence of radiation exposure. Especially, radiation exposure has side effects on children and pregnant women. Compared to the invasive IR technique, HIFU is a promising treatment for pediatric tumors. HIFU is safer and more effective in improving treatment efficacy using a monitoring device. However, the development of treatment process for the brain, eye, and thyroid is yet to achieve technical maturity because of their unique locations.[40] If a complication occurs after surgery, it is vital to evaluate the skin surface to address treatment-related burns, monitor important signs of nerve burns, evaluate for bone fractures, and administer pain relief drugs if necessary.

(7) Uterine fibroid or adenomyosis

Patients with uterine fibroids or adenomyosis usually experience menorrhagia, abnormal vaginal discharge, increase in bloody discharge, and dysmenorrhea, accompanied with subfertility.[41] The goal of HIFU treatment for uterine fibroids and adenomyosis is to alleviate symptoms, induce necrosis, and decrease its volume.[42] MRI is used for the assessment of remission of clinical symptoms. HIFU is considered a low risk procedure because it does not require incisions on the body for the treatment. Skin preparation, including shaving, cleaning, degreasing, and degassing is an important step for a successful HIFU therapy.[43] Presence of hair, dirt, or grease on the skin surface of the target tumor can cause deflection leading to accidental skin burns. Uterine fibroids and adenomyosis treatments are performed under intravenous sedation. We can continuously communicate with the patient when she experiences pain, nausea, or other symptoms during treatment; the operator will recheck therapeutic parameters or revise the treatment slice. Preliminary imaging evaluation plays an important role in treatment planning, especially for assessing optimal acoustic window and identifying the targeted volume that should be kept away from air, cavity organ, and non-targeted bone in the energy path which can reflect or absorb ultrasound. HIFU treatment is effective, safe, and non-invasive in treating symptomatic uterine fibroids and adenomyosis. The greatest advantage of HIFU when compared to that of surgery is its ability to conserve or improve fertility by UAE, especially for women who desire to get pregnant.[44] HIFU provides a first-line treatment for patients with uterine fibroids and adenomyosis who desire pregnancy.[45] The side effects and complications include abdomen pain, skin burns, paresthesia of the leg because of the nerve damage, uterine inflammation, bowel perforation, and so on; however, the complication rate is only 1.6%. HIFU has been generally accepted as a treatment for patients with uterine fibroids or adenomyosis.

(8) Breast cancer and fibroadenomas

Breast cancer is found at the early stage due to its accurate diagnosis by MRI/magnetic resonance spectroscopy. Breast fibroadenomas (FA) are the most common benign tumors, which account for about 70% of benign breast lesions.[46] They usually affect females in the reproductive period who have no other obvious symptoms except for a palpable breast lump during self-examination, occasionally associated with breast pain. A large number of patients choose breast-conserving therapy. As a conservative treatment, HIFU proceeds without surgical scars and seems to be easily accepted among younger patients. However, in some patients who opt for surgical excision, it may result in scar, local skin collapse, and nipple displacement. Minimally invasive cryoablation has been accepted because of its excellent efficacy and safety. Other thermoablation methods such as radiofrequency, laser, or microwave ablation are more frequently used in breast cancer patients. HIFU can precisely deliver energy to the targeted area without destroying skin integrity. Some studies have shown that HIFU ablation of a FA was feasible and effective. Some studies showed that the volume of FA reduced in 43.5% of patients after 6 months of HIFU treatment and in 72.5% of patients during the 1-year follow-up. Currently, data is lacking in evaluating the effectiveness of time and persistence of volume reduction. Other studies have shown a stable volume reduction of 77.32–90.47% at 1–2-year follow-up after HIFU treatment.[47] Complete ablation of HIFU in breast cancer was found in 65% of patients, and the local recurrence rate was 4.2%. The most common complications are skin burns, necrosis, seroma, and ecchymosis. Overall, HIFU is a promising, effective, safe, and well-tolerated, treatment option with a high level of patients' satisfaction. HIFU is an alternative treatment option in patients with breast FA.

## 5. Assessment methods before and after HIFU

In combination with functional MRI, MRI provides a very accurate assessment of HIFU ablation extent. The only disadvantage of HIFU is the lack of a biopsy sample that can be histopathologically examined. We usually perform MRI to identify tumor quality and location and measure its size and extent to avoid the risk path before HIFU. Most of the tumors can be classified as benign or malignant. MRI shows a lack of contrast perfusion, a higher signal on T1WI images, a lower signal on T2WI images after HIFU, and a thin rim high signal at the periphery of the treated area on T2WI images, which indicates tissue coagulative necrosis. Residual tumor is observed clearly on MRI after HIFU; therefore, it could be performed to assess the extent of the treated and residual lesion. Treated tumor volume has a negative correlation with the recurrence of the tumor. Before HIFU treatment, absolute enhancement of the tumor is investigated on enhanced MRI. If there is a residual tumor that is seen as a nodular or irregular enhancement at the edge of the treated area after treatment on MRI scans, it shows a rapid enhancement and early washout. Some benign diseases such as edema and inflammation also show a thin rim on T2WI images and enhancement on contrast enhanced MRI. The ablation tissue volume occupied the whole tumor volume was considered as a complete ablation in which the residual tumor occupied less than 10%. In clinics, complete ablation is attempted. If a residual tumor is occupying more than 10%, which is an incomplete ablation, recurrence is expected to occur.[48] Some tumors are resected after HIFU treatment for 2–20 months. We must ablate a solid malignant tumor from the surrounding normal tissue within a margin of 0.5–2.0 cm.[49] Another evaluation is the improvement of symptoms after HIFU, including pain relief and tumor control. We usually use a visual analog scale (VAS) to evaluate the pain score. VAS ranges from 0 to 10, with 0 denoting the absence of pain and 10 denoting the worst pain. Some questionnaires are available for the assessment of the quality of life including physical, mental, and social state. Activities of daily living scale include the assessment of transferring, dressing, sitting, walking, bathing, using the toilet, controlling stool and urine, and using chair and transport. The functional independence measurement screening can absolutely assess the capacity of daily living.

## 6. Discussion

As a generally accepted interventional technology, HIFU is a promising, effective, non-invasive modality for the treatment of solid tumors, including benign and malignant tumors of the breast, liver, pancreas, uterus, bone, kidney, prostate, thyroid, and brain. Particularly, it is being used increasingly for the treatment of uterine fibroids and adenomyosis. Over the last 10 years, a growing number of clinical trials have examined the effect and efficacy of HIFU treatment.

They have shown that HIFU has a wide range of indications, and it has become an important alternative or adjunct to current standard treatments, including surgery, radiation, gene therapy, immunotherapy, and chemotherapy. MRgHIFU has a higher cost; however, it is more accurate than USgHIFU, particularly with regard to the application of anatomic details. MRgHIFU has temperature mapping which monitors the extent of necrosis of the targeted tissue. HIFU is safe, has lesser complications, and is an effective treatment modality. The only disadvantage of HIFU is that it is more time-consuming for tumor treatment than RFA. In the future, lower energy HIFU treatments may play a significant role in mediating targeted drug and gene delivery for cancer treatment. In this article, we mainly introduce indications, applications, complications, and assessments of the HIFU system. HIFU is recommended as an effective treatment not only for cancer but also for inflammatory diseases. Although studies have demonstrated high percentages of complete ablation, complete pathological ablation is not obtained in all patients. Therefore, this technique should be further developed in order to reduce the time consumed for the treatment. Immobilization of patients is very important to ensure that the treatment is delivered at the correct location. Breathing movements are difficult to control and should be reduced to a minimum by some methods during treatment. General anesthesia is not ideal as this is associated with additional complications, requires an anesthetist, and prolongs the hospital stay of the patient. Local anesthesia was found to be inadequate, resulting in patient movement during the procedure. Conscious sedation, pectoralis major block, or a combination of local anesthesia techniques might be more effective in pain reduction, ensuring patient comfort and relaxation during treatment. In addition, a well-designed position covering the entire breast is recommended to reduce movements caused by breathing or the heart. Real-time imaging is very important to visualize the tumor, follow the progress of the treatment, and be able to amend the treatment when necessary. If the quality of the imaging is not good enough, the lesion will be missed on the imaging monitor and pathological complete ablation will be difficult to obtain. In the future, these difficulties need to be solved, which can lead to HIFU being used more widely in practice.

In conclusion, HIFU is an indispensable complementary therapy, which needs to be combined with other treatments like chemotherapy, surgery, or minimally invasive IR techniques for the management of malignant tumors. More importantly, it can decrease tumor burden, lower the clinical stage and increase the resection rate of cancer, especially among the elderly and children, due to fewer complications, rapid rehabilitation rates, and shorter hospitalization time. For patients with uterine fibroids or adenomyosis desiring pregnancy, HIFU is the first choice of treatment. Patients with benign tumors not only choose surgery but also HIFU, because it can preserve organ integrity and function. Additional clinical studies are needed to confirm and evaluate the role of HIFU.

## Declaration of competing interest

All the authors declare that they have no competing financial interests or personal interests relationships that may have appeared to influence the work reported in this paper.

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