CODEN [USA]: IAJPBB ISSN : 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES
SJIF Impact Factor: 7.187

Online at: http://www.iajps.com *Review Article*

EFFECTS OF LOW INTENSITY BIO-RESONANCE FOCUSED ULTRASOUND ON DESTROYING CANCEROUS CELLS: A LITERATURE REVIEW

Dr. Raymond L Venter
([1]BSC, [2]Honorary Doctorate)
[1]Quantum University
[2]University of Southampton UK

Article Received: April 2021 **Accepted:** April 2021 **Published:** May 2021

Abstract:
The literature describing low-intensity ultrasound in two significant areas of cancer therapy - sonodynamic therapy and ultrasound-mediated chemotherapy - was reviewed. Each technique consistently killed cancer cells, and the bioeffects of ultrasound were attributed primarily to thermal actions and inertial cavitation. Each therapeutic modality benefited from using theranostic contrast agents composed of microbubbles for both therapy and vascular imaging. The development of these agents is critical because it establishes a therapeutic-diagnostic platform for monitoring anti-cancer therapy success. However, little attention has been paid to either the direct examination of the underlying mechanisms underlying observed bioeffects or the viability of these therapies in naturally occurring cancers in larger mammals; if such investigations yielded encouraging results, a therapy technique could be rapidly applied in treating cancer patients.

Keywords: *Ultrasound bioeffects, Cancer therapy, Low-intensity ultrasound, Sonodynamic therapy, Antivascular ultrasound, ultrasound-mediated chemotherapy.*

Corresponding author:
Dr. Raymond L Venter, *
Quantum University
University of Southampton UK

QR code

Please cite this article in press Raymond L Venter., ***Effects Of Low Intensity Bio-Resonance Focused Ultrasound On Destroying Cancerous Cells: A Literature Review.,*** *Indo Am. J. P. Sci, 2021; 08(05).*

INTRODUCTION:

Ultrasound therapy with low intensity has been used to treat a variety of conditions. It has been used in conjunction with sensitizing molecules to affect cancer cells (sonodynamic therapy) directly; it has been used in conjunction with chemotherapeutic molecules to enhance their activity in cancer therapy (ultrasound-mediated chemotherapy); it has been used to affect cells and their components (sonoporation) directly; it has been used for gene delivery or transfection, as well as to promote cell growth (ultrasound-mediated cell growth). This review aims to shed light on the role of low-intensity ultrasound in cancer treatment. The published studies investigated in vitro cancer cell suspensions and cultures and the treatment of various implanted tumours in small laboratory animals. The following review discusses four of the most frequently used low-intensity ultrasound applications in cancer therapy research: sonodynamic therapy, ultrasound-mediated chemotherapy, ultrasound-mediated gene delivery, and anti-vascular ultrasound therapy.

Although no widely accepted definition of low-intensity ultrasound exists, this review focused on studies in which cancer cells or tumours were generally insonated at a power density less than 5.0 W.cm2, which corresponds to a root-mean-square pressure amplitude of approximately 0.3 MPa. Numerous variables in the sonication conditions used in the literature complicate accurate comparisons between reports. Pressure-intensity conversions were performed in this review using the formula I = p2/c, where I denote intensity, p denotes root mean square pressure amplitude, = density, and c denotes sound speed (Preston 1991).

In general, insonation of neoplasms with low-intensity ultrasound is a straightforward procedure because it does not require a focused beam (which must be precisely located), the apparatus is relatively inexpensive, the bioeffects on adjacent normal tissues are generally believed to be minimal, and it is possible to easily target sensitizing or chemotherapeutic molecules and microbubbles located within the neoplasm. Although treatment times are longer than with focused high-intensity ultrasound, repeated treatments or dose fractionation are straightforward to perform.

Sonodynamic Therapy

Sonodynamic therapy is derived from the term photodynamic therapy. Unlike photodynamic therapy, which uses light to stimulate photosensitizers to generate reactive oxygen species directly, sonodynamic therapy uses ultrasound-induced cavitation and sonosensitizers to generate free radicals that kill nearby rapidly dividing cancer cells. An advantage of sonodynamic therapy is that it uses continuous, low-intensity ultrasound at diagnostic ultrasound frequencies to treat tumours located deep within the body. On the other hand, photodynamic therapy employs visible light, which rapidly attenuates in tissues and penetrates only superficially or intraoperatively. When Jin et al. (2000) treated a subcutaneously located murine squamous cell carcinoma, they discovered that sonodynamic therapy inhibited tumour growth by 77%, compared to 27% with photodynamic therapy. The latter was ineffective in the tumour's deeper regions.

Sonodynamic therapy was initially based on the same light-sensitive agents developed for photodynamic therapy, hematoporphyrin and its derivatives. A sensitizing agent should be taken up and retained preferentially by the tumour. The therapy kills cancer cells while having a negligible effect on normal tissues in the surrounding area; the agent should also be relatively non-toxic to normal mammalian tissues. To maximize the efficacy of treating solid tumours, the sonosensitizer must be injected intravenously before insonation, rather than directly into the tumour, to ensure that it is distributed more completely and uniformly throughout the neoplasm (Ninomiya et al. 2012).

There have been published overviews of the sonosensitizers used in the therapy (Kuroki et al., 2007; Feril et al., 2011; Shibaguchi et al., 2011; Chen et al., 2014). In sonodynamic therapy, the sonication parameters (typically 1.0-2.0 MHz at a power density of 0.5 to 3.0 W.cm2; Tables 1,2) are chosen to induce inertial cavitation in cell culture or tumour, a process in which a bubble in a liquid rapidly collapses, generating a shock wave that generates free radicals and initiates a cascade of molecular events that activate the sonosensitizer and damage the cancer cells (Misik and Riesz 2000; Rosenthal et al. 2004; Yu et al. 2004[c]). While it appears that the production of reactive oxygen species plays a role in the antitumor effect, Wang et al. 2011[a] state that thermal effects cannot be ruled out. Along with these direct cytotoxic effects on neoplastic cells, it is necessary to consider other possible effects on the growing tumour, such as its vascular supply. According to Gao et al. (2013), sonodynamic therapy also had an antivascular effect, inhibiting tumour neovascularization. Additionally, a chemotherapeutic agent has been used as the sonosensitizer. Adriamycin (Gao et al. 2010), cisplatin (Bernard et al. 2011; 2012 [0.4 0.02 MPa]), and

doxorubicin (Liang et al. 2013) were found to be cytostatic in vitro, and their apoptotic activity was enhanced when combined with chlorine e6 (Gao et al. 2010) or a hematoporphyrin (Liang et al. 2013).

Table 1: Sonodynamic therapy of cell cultures and suspensions

Cancer cell culture/suspension	Sonosensitizer	Insonation parameters		Reference
		MHz	W.cm−2	
(viii) non-neoplastic (endothelial cells)	5-aminolevulinic acid	1.0	1.0	Gao et al 2013
multiple cell lines	porphyrin derivative	1.0	1.0	Tsuru et al 2012
multiple cell lines	porphyrin derivative	1.0	0.5-2.0	Hachimine et al 2007
tongue	5-aminolevulinic acid	1.0	0.6, 0.8	Lv et al 2012
murine mammary	chlorine e6	1.0	0.36, 0.72	Li et al 2013
murine leukemia	protoporphyrin IX	1.1	0.64-2.1	Wang et al 2013[b]
histiocytic lymphoma	hematoporphyrin	1.1	1.0	Su et al 2013[a]
human melanoma	cisplatin	1.0	1.0	Bernard et al 2012
human leukemia	protoporphyrin IX	1.1	1.0	Su et al 2014
gastric	antibody/porphyrin	1.0	1.0	Abe et al 2002
Ehrlich ascites	protoporphyrin IX	1.34	1.0-5.0	Zhao et al 2009
acute myeloid leukemia	chlorine e6	1.1	1.0	Su et al 2013[b]
cholangiocarcinoma	Hematoporphyrin + doxorubicin	1.2	0.5-2.0	Liang et al 2013
ovarian	cisplatin	1.0	2.0	Bernard et al 2011
ovarian	methylene blue	1.7	0.46	Xiang et al 2011

human breast	protoporphyrin IX	1.1	1.0	Li et al 2012[a]
	chlorin e6	1.0	0.36, 0.72	Wang et al 2013[a]
	chlorin e6 + adriamycin	1.0	0.5-2.0	Gao et al 2010
glioma	ZnPcS2P2	1.0	0.5	Chen et al 2012[b]
	HMME	1.0	0.5	Li et al 2013
	photofrin	1.0	0.5	Xu et al 2012
	II	1.0	0.5	Xu et al 2013
	titanium nanoparticles	1.0	1.0	Yamaguchi et al 2011[b]
nasopharyngeal	curcumin	1.7	0.46	Wang et al 2011[b]
	II	1.7	0.46	Wang et al 2011[c]
	II	1.7	0.46	Wang et al 2012[b]
hepatic	hematoporphyrin	1.92	1.27-3.18	Yumita et al 1989
	II	1.43	1.0-4.0	Liu et al 2008[b]
	titanium nanoparticles	1.0	0.1	Ninomiya et al 2012
	II	0.5,1.0	0.8, 0.4	Ninomiya et al 2014
	hypocrellin-B	1.7	0.46	Wang et al 2012[a]

HMME = hematoporphyrin monomethyl ether

Table 2: Sonodynamic therapy of tumors

Tumor	Sonosensitizer	Insonation parameters		Reference
		MHz	W.cm−2	
human MKN-45	DCPH-PNa(I)	1.0	2.0	Hachimine et al 2013
tongue	5-aminolevulinic acid	1.1	2.0	Gao et al 2013
small cell lung	chlorin e6	1.0	0.4-1.6	Chen et al 2013[b]
osteosarcoma (rats)	hematoporphyrin	10.5	0.8	Tian et al 2009
squamous cell	gallium-porphyrin/pheophorbide-a	1.0	0.51	Jin et al 2000
gastric	antibody / gallium-porphyrin	1.0	2.0	Abe et al 2002
	porphyrin derivative	1.0	2.0	Tsuru et al 2012
breast	photofrin	.015/1.0	0.2,2.0	Barati et al 2010
	no sensitizer	.015/1.0	0.2,2.0	Barati et al 2009
glioma (rats)	5-aminolevulinic acid	1.04	10.0	Ohmura et al 2011
	5-aminolevulinic acid	1.0	2.65	Jeong et al 2012
	chlorin e6/polyvinyl pyrrolidone	1.0	0.4-1.0	Tserkovsky et al 2012
hepatic	hematoporphyrin	1.43	2.0	Liu et al 2008[b]
	protoporphyrin IX	1.43	3.0	Wang et al 2011[a]
		1.0	1.0	Ninomiya et al 2012

	titanium oxide nanoparticles			Zheng et al 2012
	hematoporphyrin microbubbles	1.0	2.0	Shi et al 2011
	Chlorin e6	1.56	4.0	
colon	ATX-S10	2.0	3.0	Yumita et al 2000[a]
	photofrin II	1.92	1.0-5.0	Yumita et al 2000[b]
	protoporphyrin IX/nanoparticles	1.1	2.0	Sazgarnia et al 2011
	protoporphyrin IX/nanoparticles	1.1	2.0	Shanei et al 2012
	NPe6	2.0	3.0	Yumita et al 2011
	polyhydroxy fullerenes	2.0	3.0	Yumita et al 2013
murine sarcoma 180	hematoporphyrin	1.92	1.7	Yumita et al 1990
	pheobromide a	1.92	3.0	Umemurra et al 1996[b]
	protoporphyrin IX	2.2	5.0	Liu et al 2007[a,b]
	sinoporphyrin sodium	1.9	2.0-6.0	Li et al 2013

Unless otherwise stated all tumors were in mice. Key: ATX-S10 = 4-formyloxim ethylidene-3-hydroxy-2-vinyl-deuterio-porphynyl(IX)-6,7-d'aspartic acid; NPe6 = mono-l-aspartyl chlorin e6

Following Yumita et al. (1989) .'s and Umemura et al. (1990) .'s initial descriptions of sonodynamic therapy, numerous confirming reports further demonstrated the therapy's bioeffects. In contrast to previous reviews, we have classified the research studies according to the type of cancer cell and the associated sonsensitizer that were insonated; this was done to serve as a guide for previous sonodynamic studies that place a premium on the type of cancer receiving therapy (Tables 1,2). Over the last 25 years, actual data have been published using various sonosensitizers and involving various types of cancer (Tables 1,2), and each report has consistently demonstrated the significant bioeffects of sonodynamic therapy. However, determining the relative merits of each of these numerous sonodynamic agents is difficult because each agent was investigated in isolation without comparison to another's efficacy. Thus, critical questions remain unanswered, such as whether the newly developed nanoparticle sonosensitizers are more effective at killing cancer cells than the original porphyrins.

Sonodynamic therapy, as a gold standard, induced apoptosis in cancer cell suspensions and cultures and inhibited tumour growth in animal models of cancer.

The therapy's efficacy has also been demonstrated in tumours that are more deeply located, such as those of the central nervous system (Ohmura et al., 2011; Gao et al., 2013; Jeong et al., 2012). Histologic examinations of post-therapy cancer cells consistently revealed damage to their ultrastructure, including the destruction of cell membranes, mitochondrial swelling, and chromatin condensation (Liu et al. 2006[b], 2007[a, b], 2008; Wang et al. 2008[a], 2011[c], 2012[b]); it was assumed that these changes induced by the therapy mediated cancer cell death. Combining photodynamic and sonodynamic therapy had a synergistic effect in solid tumours, resulting in increased post-treatment tumour necrosis, tumour growth inhibition, and increased survival times (Jin et al. 2000; Tserkovsky et al. 2012).

Given that many of the intravenously injected sonosensitizers (Tables 1, 2) were initially developed for use in photodynamic therapy, those used in sonodynamic therapy in the future must be light insensitive or have no cutaneous side effects (Shibaguchi et al. 2011; Ninomiya et al. 2012; Tsuru et al. 2012; Gao et al. 2013). Preliminary data from solid tumours support the administration of a regimen of multiple therapies to enhance bioeffects and reduce tumour growth and size; fractionation will also help mitigate the thermal effects of therapy (Jeong et al., 2012).

Combining the sonosensitizer with a microbubble contrast agent could significantly enhance sonodynamic therapy in the future (Zheng et al., 2012). The combined agent is then a theranostic agent. Ultrasound imaging can be used to monitor the microbubbles' entry into the tumour vasculature and, once detected within the tumour via diagnostic ultrasound, sonodynamic therapy can be initiated. The establishment of a therapeutic-diagnostic platform capable of monitoring the efficacy of therapy (Lionetti and Paddeu 2010). Additionally, insonation of the microbubble may have significant local thermal bioeffects, including the destruction of endothelial cells lining the tumour vasculature and a reduction in tumour vascularity (Levenback et al. 2012).

To date, in vivo observations have been made on laboratory animals (mice and rats) implanted with subcutaneous tumours, indicating the need for future studies in a larger mammal, possibly using sonodynamic therapy to treat naturally occurring cancers. These additional studies, if successful, could result in the start of human clinical trials.

Ultrasound Along with Chemotherapy

There is interest in using low-intensity ultrasound to enhance the delivery of chemotherapeutic agents to solid tumours in cancer therapy. Agents may be non-specific in that they do not target only malignant cells, and thus high concentrations of the cytotoxic drug will be present in normal tissues, possibly causing adverse effects (Nomikou et al. 2010 [a]). Additionally, factors such as poor vascularity and defective lymphatic drainage can result in elevated interstitial fluid pressure within the tumour, preventing the drug from being absorbed in therapeutic levels (Nomikou et al. 2010 [a]). Insonation of a tumour in the presence of a chemotherapeutic agent has the potential to improve the agent's delivery to cancer cells while minimizing cytotoxicity in adjacent normal tissues. Chemotherapeutic agents have been delivered using ultrasound alone, ultrasound combined with microbubbles and drug-loaded microbubbles. Additional chemotherapeutic studies have been conducted with drug-loaded liposomes in the presence of microbubbles and ultrasound and drug-loaded liposomes attached to microbubbles.

Along with the role of microbubbles in chemotherapy delivery via these direct effects, other antivascular effects have been described, which will be discussed later (see Anti Vascular Ultrasound). Additionally, magnetic microbubbles have been developed in which the drug and iron oxide are combined into a microbubble that can be imaged using both ultrasound and magnetic resonance (MR) imaging. This review has concentrated on the findings of recent research studies; for a broader overview of the subject, the reader is referred to Nomikou and McHale's 2010[b] and Trendowski's 2010[c] papers (2013).

LIFU in the presence of chemotherapy

Low-intensity ultrasound has been investigated in vitro and in vivo for its potential to increase cancer cells' sensitivity to a chemotherapeutic agent.

***In vitro* studies**

Insonation of tumour cell suspensions and cultures in the presence of a chemotherapeutic agent can facilitate the agent's cellular uptake; the inertial cavitation caused by the ultrasound beam results in the formation of microjets that carry the agent directly into the cell or disrupt the cell membranes, allowing extracellular agents to enter (Feril and Tachibana 2012).

Yoshida et al. (2008) observed a synergistic enhancement of cell killing and increased apoptosis in human myelomonocytic cells when they were insonated in the presence of doxorubicin. Few studies have compared the responses of chemosensitive and

chemoresistant cancer cells. Yu et al. (2004[a]) identified sub-strains of human ovarian cancer cell lines resistant to Adriamycin and Cisplatin. They discovered that chemosensitive and chemoreceptive cells exhibit distinct biochemical properties. Ultrasound inhibited cell proliferation and clone formation in chemoresistant cell populations, but not in chemosensitive cells. Hassan et al. (2012) examined human uterine carcinoma cells and a multidrug-resistant phenotype in another doxorubicin study. The order in which insonation and doxorubicin were applied revealed differences in the carcinoma cells' sensitivity. The authors observed that depending on the sonication time, the parent carcinoma cells could be desensitized, or the resistant cell could be sensitized to doxorubicin. On scanning electron microscopy, insonation of human tongue carcinoma cells in the presence of scutellarin significantly enhanced cell injury with irregularly shaped and fractured microvilli and the formation of apoptotic bodies; there was a decrease in cancer cell growth and an increase in cell apoptosis (Li et al. 2013).

***In vivo* studies**

Chemotherapy and ultrasound efficacy have also been studied in mouse tumour models. Tomizawa et al. (2001) discovered that combining intraperitoneal bleomycin with ultrasound results in tumour growth suppression in a murine lymphoma. When camptothecin was injected directly into a fibrosarcoma and then insonated, it was hypothesized that the resulting decrease in tumour growth was due to the chemotherapeutic drug being distributed throughout the tumour via ultrasound including the less vascularized regions (Nomikou et al. 2010[a]). Chemosensitive and chemoresistant ovarian cancers were implanted in the murine kidney and insonated 15 minutes after adriamycin was injected intraperitoneally (Yu et al. 2004[b]). Because ultrasound enhanced adriamycin in both types of cancer, it was hypothesized that ultrasound could reverse adriamycin resistance in ovarian cancer cells. Scutellarin was administered orally before tumour insonation in studies on a human tongue squamous cell carcinoma, and the combined therapy inhibited tumour growth, angiogenesis, and lymphangiogenesis (Li et al., 2013).

The RoyalVibe.Focused Ultrasound Device

Dr Raymond Venter is a scientist with an entrepreneurial spirit. He is the inventor and manufacturer of the CellQuicken device and the sole director of the CellQuicken company. Raymond invented the CellQuicken frequency generator, which instantly cured his father of cancer.

It is a natural sound frequency device that assists the body in cellular restoration. The device employs low-intensity ultrasound with a high frequency and energy levels at the cellular level. This therapy takes place while you sleep, work at a desk, or rest: there is no medication involved, and there are no side effects. Focused ultrasound is a development of modern technology that allows for the treatment of conditions without the side effects associated with conventional treatments. However, we have evolved only when we address the underlying cause of the condition rather than merely masking the symptoms.

CellQuicken's Focused Ultrasound product solutions determine the cell resonance frequency to stimulate or destroy the bioenergy contained within the cell or organism.

Focused ultrasound is a relatively new technology that directs acoustic energy to anatomical targets to minimise hidden pathologies. While conventional allopathic medicine is effective in treating various diseases, it is ineffective in treating several cancers.

Ultrasound technology's continued advancement should be closely monitored and considered a viable alternative to conventional treatment, which frequently involves severe side effects and invasive procedures.

CONCLUSION:

All of the therapies that used low-intensity ultrasound, including sonodynamic therapy, ultrasound-mediated chemotherapy and gene delivery, and anti vascular ultrasound therapy, consistently produced bioeffects that resulted in the death of cancer cells. Low-intensity ultrasound applications are thought to be safe and non-toxic, easy to apply to a tumour, and relatively inexpensive. Multiple bioeffects are likely responsible for a therapy's efficacy, although the importance of thermal and inertial cavitation bioeffects has been established in animal tumour models. In some cases, the tumour's accessibility to insonation is a constraint, as the cancer cells may be adjacent to a gas-containing structure or bone and thus difficult to reach by the ultrasound beam. This limitation can be overcome in such clinical situations by imaging and treating with intracavity transducers.

Additionally, the current generation of microbubbles has a limited capacity for therapeutic loading agents at the required dosages. These limitations could be overcome by optimizing the design of microbubbles to increase their payload carrying capacity. Co-administration of therapeutic agents and microbubbles could also be used to circumvent the payload issue.

REFERENCES:

1. Raymond L Venter., Environmental Energy For Cellular Growth And Repair Especially By Bio-Resonance Focused Ultrasound: A Literature Review., Indo Am. J. P. Sci, 2021; 08(04).
2. Raymond L Venter., Role Of Bio-Resonance Focused Ultrasound On Stem Cell Proliferation And Growth: A Review.., Indo Am. J. P. Sci, 2021; 08(04).
3. Irene H James., Cellular Destruction From Environmental Energy Exposure Especially By Cell Phones And Mobile Internet.., Indo Am. J. P. Sci, 2021; 08(04).
4. Raymond L Venter., Focused Ultrasound Involving The Usage Of Cell Resonance To Understand The Effect And Its Use As A Therapy For Disease Modification.,Indo Am. J. P. Sci, 2021; 08(03).
5. Abe H, Kuroki M, Tachibana K, Li T, Awasthi A, Ueno A, Matsumoto H, Imakiire T, Yamauchi Y, Yamada H, Ariyoshi A, Kuroki M. Targeted sonodynamic therapy of cancer using a photosensitizer conjugated with antibody against carcinoembryonic antigen. Anticancer Res. 2002;22:1575–1580. [PubMed] [Google Scholar]
6. Al-Mahrouki AA, Karshafian R, Giles A, Czarnota GJ. Bioeffects of ultrasound-stimulated microbubbles on endothelial cells: gene expression changes associated with radiation enhancement in vitro. Ultrasound Med Biol. 2012;38:1958–1969. [PubMed] [Google Scholar]
7. Anderson CR, Hu X, Zhang H, Tlaxca J, Decléves AE, Houghtaling R, Sharma K, Lawrence M, Ferrara KW, Rychak JJ. Ultrasound molecular imaging of tumor angiogenesis with an integrin targeted microbubble contrast agent. Invest Radiol. 2011;46:215–224. [PMC free article] [PubMed] [Google Scholar]
8. Aryal M, Vykhodtseva N, Zhang YZ, Park J, McDannold N. Multiple treatments with liposomal doxorubicin and ultrasound-induced disruption of blood-tumor and blood-brain barriers improve outcomes in a rat glioma model. J Control Release. 2013;169:103–111. [PMC free article] [PubMed] [Google Scholar]
9. Baker KG, Robertson VJ, Duck FA. A review of therapeutic ultrasound: biophysical effects. Phys Ther. 2001;81:1351–1358. [PubMed] [Google Scholar]
10. Bai WK, Shen E, Hu B. The induction of the apoptosis of cancer cell by sonodynamic therapy: a review. Chin J Cancer Res. 2012[a];24:368–373. [PMC free article] [PubMed] [Google Scholar]
11. Bai WK, Wu ZH, Shen E, Zhang JZ, Hu B. The improvement of liposome-mediated transfection of pEGFP DNA into human prostate cancer cells by combining low-frequency and low-energy ultrasound with microbubbles. Oncol Rep. 2012[b];27:475–480. [PubMed] [Google Scholar]
12. Barati AH, Mokhtari-Dizaji M, Mozdarani H, Bathaie SZ, Hassan ZM. Treatment of murine tumors using dual-frequency ultrasound in an experimental in vivo model. Ultrasound Med Biol. 2009;35:756–763. [PubMed] [Google Scholar]
13. Barati AH, Mokhtari-Dizaji M. Ultrasound dose fractionation in sonodynamic therapy. Ultrasound Med Biol. 2010;36:880–887. [PubMed] [Google Scholar]
14. Bernard V, Fojt L, Skorpíková J, Mornstein V. Determination of free cisplatin in medium by differential pulse polarography after ultrasound andcisplatin treatment of a cancer cell culture. Indian J Biochem Biophys. 2011;48:59–62. [PubMed] [Google Scholar]
15. Bernard V, Mornstein V, Škorpíková J, Jaroš J. Ultrasound and cisplatin combined treatment of human melanoma cells A375--the study of sonodynamic therapy. Ultrasound Med Biol. 2012;38:1205–1211. [PubMed] [Google Scholar]
16. Bunte RM, Ansaloni S, Sehgal CM, Lee WM, Wood AK. Histopathological observations of the antivascular effects of physiotherapy ultrasound on a murine neoplasm. Ultrasound Med Biol. 2006;32:453–461. [PubMed] [Google Scholar]
17. Burgess A, Hynynen K. Drug delivery across the blood-brain barrier using focused ultrasound. Expert Opin Drug Deliv. 2014;11:711–721. [PMC free article] [PubMed] [Google Scholar]
18. Burke CW, Price RJ. Contrast ultrasound targeted treatment of gliomas in mice via drug-bearing nanoparticle delivery and microvascular ablation. J Vis Exp. 2010:46. doi:pii: 2145. 10.3791/2145. [PMC free article] [PubMed] [Google Scholar]
19. Burke CW, Klibanov AL, Sheehan JP, Price RJ. Inhibition of glioma growth by microbubble activation in a subcutaneous model using low duty cycle ultrasound without significant heating. J Neurosurg. 2011;114:1654–61. [PMC free article] [PubMed] [Google Scholar]
20. Carson AR, McTiernan CF, Lavery L, Hodnick A, Grata M, Leng X, Wang J, Chen X, Modzelewski RA, Villanueva FS. Gene therapy of carcinoma using ultrasound-targeted microbubble destruction. Ultrasound Med Biol. 2011;37:393–402. [PMC free article] [PubMed] [Google Scholar]

21. Carson AR, McTiernan CF, Lavery L, Grata M, Leng X, Wang J, Chen X, Villanueva FS. Ultrasound-targeted microbubble destruction to deliver siRNA cancer therapy. Cancer Res. 2012;72:6191–6199. [PMC free article] [PubMed] [Google Scholar]
22. Chang S, Guo J, Sun J, Zhu S, Yan Y, Zhu Y, Li M, Wang Z, Xu RX. Targeted microbubbles for ultrasound mediated gene transfection and apoptosis induction in ovarian cancer cells. Ultrason Sonochem. 2013;20:171–179. [PMC free article] [PubMed] [Google Scholar]
23. Chen CC, Sheeran PS, Wu SY, Olumolade OO, Dayton PA, Konofagou EE. Targeted drug delivery with focused ultrasound-induced blood-brain barrier opening using acoustically-activated nanodroplets. J Control Release. 2013;172:795–804. [PMC free article] [PubMed] [Google Scholar]
24. Chen JJ, Chen JJ, Chiang CS, Hong JH, Yeh CK. Assessment of tumor vasculature for diagnostic and therapeutic applications in a mouse model in vivo using 25-MHz power Doppler imaging. Ultrasonics. 2011;51:925–931. [PubMed] [Google Scholar]
25. Chen JJ, Fu SY, Chiang CS, Hong JH, Yeh CK. Characterization of tumor vasculature distributions in central and peripheral regions based on Doppler ultrasound. Med Phys. 2012[a];39:7490–7498. [PubMed] [Google Scholar]
26. Chen JJ, Fu SY, Chiang CS, Hong JH, Yeh CK. A preclinical study to explore vasculature differences between primary and recurrent tumors using ultrasound Doppler imaging. Ultrasound Med Biol. 2013[a];39:860–869. [PubMed] [Google Scholar]
27. Chen Z, Li J, Song X, Wang Z, Yue W. Use of a novel sonosensitizer in sonodynamic therapy of U251 glioma cells in vitro. Exp Ther Med. 2012[b];3:273–278. [PMC free article] [PubMed] [Google Scholar]
28. Chen H, Zhou X, Gao Y, Zheng B, Tang F, Huang J. Recent progress in development of new sonosensitizers for sonodynamic cancer therapy. Drug Discov Today. 2014 Jan 30;pii:S1359–6446. [PubMed] [Google Scholar]
29. Chen B, Zheng R, Liu D, Li B, Lin J, Zhang W. The tumor affinity of chlorin e6 and its sonodynamic effects on non-small cell lung cancer. Ultrason Sonochem. 2013[b];20:667–673. [PubMed] [Google Scholar]
30. Chin CT, Raju BI, Shevchenko T, Klibanov AL. Control and reversal of tumor growth by ultrasound activated microbubbles. IEEE International Ultrasonics Symposium Proceedings. 2009:77–80. [Google Scholar]
31. Chumakova OV, Liopo AV, Evers BM, Esenaliev RO. Effect of 5-fluorouracil, Optison and ultrasound on MCF-7 cell viability. Ultrasound Med Biol. 2006;32:751–758. [PubMed] [Google Scholar]
32. Cochran MC, Eisenbrey J, Ouma RO, Soulen M, Wheatley MA. Doxorubicin and paclitaxel loaded microbubbles for ultrasound triggered drug delivery. Int J Pharm. 2011;414:161–170. [PMC free article] [PubMed] [Google Scholar]
33. Cool SK, Geers B, Roels S, Stremersch S, Vanderperren K, Saunders JH, De Smedt SC, Demeester J, Sanders NN. Coupling of drug containing liposomes to microbubbles improves ultrasound triggered drug delivery in mice. J Control Release. 2013 Dec;172:885–893. [PubMed] [Google Scholar]
34. Cosgrove D. Ultrasound contrast agents: an overview. Eur J Radiol. 2006;60:324–330. [PubMed] [Google Scholar]
35. Derieppe M, Yudina A, Lepetit-Coiffé M, de Senneville BD, Bos C, Moonen C. Real-time assessment of ultrasound-mediated drug delivery using fibered confocal fluorescence microscopy. Mol Imaging Biol. 2013;15:3–11. [PubMed] [Google Scholar]
36. Duvshani-Eshet M, Benny O, Morgenstern A, Machluf M. Therapeutic ultrasound facilitates antiangiogenic gene delivery and inhibits prostate tumor growth. Mol Cancer Ther. 2007;6:2371–2382. [PubMed] [Google Scholar]
37. Escoffre JM, Mannaris C, Geers B, Novell A, Lentacker I, Averkiou M, Bouakaz A. Doxorubicin liposome-loaded microbubbles for contrast imaging and ultrasound-triggered drug delivery. IEEE Trans Ultrason Ferroelectr Freq Control. 2013;60:78–87. [PubMed] [Google Scholar]
38. Escoffre JM, Piron J, Novell A, Bouakaz A. Doxorubicin delivery into tumor cells with ultrasound and microbubbles. Mol Pharm. 2011;8:799–806. [PubMed] [Google Scholar]
39. Fan CH, Ting CY, Lin HJ, Wang CH, Liu HL, Yen TC, Yeh CK. SPIO-conjugated, doxorubicin-loaded microbubbles for concurrent MRI and focused-ultrasound enhanced brain-tumor drug delivery. Biomaterials. 2013[a];34:3706–3715. [PubMed] [Google Scholar]
40. Fan CH, Ting CY, Liu HL, Huang CY, Hsieh HY, Yen TC, Wei KC, Yeh CK. Antiangiogenic-targeting drug-loaded microbubbles combined with focused ultrasound for glioma treatment.

Biomaterials. 2013[b];34:2142–2155. [PubMed] [Google Scholar]
41. Feril LB, Ogawa R, Tachibana K, Kondo T. Optimized ultrasound-mediated gene transfection in cancer cells. Cancer Sci. 2006;97:1111–1114. [PubMed] [Google Scholar]
42. Feril LB, Tachibana K, Kondo T, Campbell PA. Sonodynamic therapy. In: Frenkel V, editor. Therapeutic ultrasound mechanisms to applications. Nova Sciences Publishers, Inc; New York,NY: 2011. pp. 279–295. [Google Scholar]
43. Feril LB, Tachibana K. Use of ultrasound in drug delivery systems: emphasis on experimental methodology and mechanisms. Int J Hyperthermia. 2012;28:282–289. [PubMed] [Google Scholar]
44. Ferrara KW, Borden MA, Zhang H. Lipid-shelled vehicles: engineering for ultrasound molecular imaging and drug delivery. Acc Chem Res. 2009;42:881–892. [PMC free article] [PubMed] [Google Scholar]
45. Fokong S, Theek B, Wu Z, Koczera P, Appold L, Jorge S, Resch-Genger U, van Zandvoort M, Storm G, Kiessling F, Lammers T. Image-guided, targeted and triggered drug delivery to tumors using polymer-based microbubbles. J Control Release. 2012;163:75–81. [PubMed] [Google Scholar]
46. Folkman J. Angiogenesis. In: Braunwald E, Fauci AS, Kasper DL, Hauser SL, Longo DL, Jameson JL, editors. Harrison's textbook of internal medicine. Mc Graw-Hill; New York: 2001. pp. 517–530. [Google Scholar]
47. Fujii H, Matkar P, Liao C, Rudenko D, Lee PJ, Kuliszewski MA, Prud'homme GJ, Leong-Poi H. Optimization of Ultrasound-mediated Anti-angiogenic Cancer Gene Therapy. Mol Ther Nucleic Acids. 2013 May 21;2:e94. [PMC free article] [PubMed] [Google Scholar]
48. Gao ZG, Fain HD, Rapoport N. Controlled and targeted tumor chemotherapy by micellar-encapsulated drug and ultrasound. J Control Release. 2005;102:203–222. [PubMed] [Google Scholar]
49. Gao HJ, Zhang WM, Wang XH, Zheng RN. Adriamycin enhances the sonodynamic effect of chlorin e6 against the proliferation of human breast cancer MDA-MB-231 cells in vitro. J South Med Univ. 2010;30:2291–2294. [PubMed] [Google Scholar]
50. Gao Z, Zheng J, Yang B, Wang Z, Fan H, Lv Y, Li H, Jia L, Cao W. Sonodynamic therapy inhibits angiogenesis and tumor growth in a xenograft mouse model. Cancer Lett. 2013;335:93–99. [PubMed] [Google Scholar]
51. Geers B, Lentacker I, Sanders NN, Demeester J, Meairs S, De Smedt SC. Self-assembled liposome-loaded microbubbles: The missing link for safe and efficient ultrasound triggered drug-delivery. J Control Release. 2011;152:249–256. [PubMed] [Google Scholar]
52. Geis NA, Katus HA, Bekeredjian R. Microbubbles as a vehicle for gene and drug delivery: current clinical implications and future perspectives. Curr Pharm Des. 2012;18:2166–2183. [PubMed] [Google Scholar]
53. Goertz DE, Yu JL, Kerbel RS, Burns PN, Foster FS. High-frequency Doppler ultrasound monitors the effects of antivascular therapy on tumor blood flow. Cancer Res. 2002;62:6371–6375. [PubMed] [Google Scholar]
54. Goertz DE, Karshafian R, Hynynen K. Antivascular effects of pulsed low intensity ultrasound and microbubbles in mouse tumors. IEEE International Ultrasonics Symposium Proceedings. 2008:670–673. [Google Scholar]
55. Goertz DE, Karshafian R, Hynynen K. Investigating the effects of pulsed low intensity ultrasound and microbubbles in mouse tumors. IEEE International Ultrasonics Symposium Proceedings. 2009:89–92. [Google Scholar]
56. Goertz DE, Todorova M, Mortazavi O, Agache V, Chen B, Karshafian R, Hynynen K. Antitumor effects of combining docetaxel (taxotere) with the antivascular action of ultrasound stimulated microbubbles. PLoS One. 2012;7:e52307. [PMC free article] [PubMed] [Google Scholar]
57. Haag P, Frauscher F, Gradl J, Seitz A, Schäfer G, Lindner JR, Klibanov AL, Bartsch G, Klocker H, Eder IE. Microbubble-enhanced ultrasound to deliver an antisense oligodeoxynucleotide targeting the human androgen receptor into prostate tumours. J Steroid Biochem Mol Biol. 2006;102:103–113. [PubMed] [Google Scholar]
58. Hachimine K, Shibaguchi H, Kuroki M, Yamada H, Kinugasa T, Nakae Y, Asano R, Sakata I, Yamashita Y, Shirakusa T, Kuroki M. Sonodynamic therapy of cancer using a novel porphyrin derivative, DCPH-P-Na(I), which is devoid of photosensitivity. Cancer Sci. 2007;98:916–920. [PubMed] [Google Scholar]
59. Hassan MA, Furusawa Y, Minemura M, Rapoport N, Sugiyama T, Kondo T. Ultrasound-induced new cellular mechanism involved in drug resistance. PLoS One. 2012;7:e48291. [PMC free article] [PubMed] [Google Scholar]
60. Hauser J, Ellisman M, Steinau HU, Stefan E, Dudda M, Hauser M. Ultrasound enhanced endocytotic activity of human fibroblasts.

Ultrasound Med Biol. 2009;35:2084–2092. [PubMed] [Google Scholar]
61. Heath CH, Sorace A, Knowles J, Rosenthal E, Hoyt K. Microbubble therapy enhances anti-tumor properties of cisplatin and cetuximab in vitro and in vivo. Otolaryngol Head Neck Surg. 2012;146:938–945. [PMC free article] [PubMed] [Google Scholar]
62. Hu X, Kheirolomoom A, Mahakian LM, Beegle JR, Kruse DE, Lam KS, Ferrara KW. Insonation of targeted microbubbles produces regions of reduced blood flow within tumor vasculature. Invest Radiol. 2012;47:398–405. [PMC free article] [PubMed] [Google Scholar]
63. Huang P, You X, Pan M, Li S, Zhang Y, Zhao Y, Wang M, Hong Y, Pu Z, Chen L, Yang G, Guo Y. A novel therapeutic strategy using ultrasound mediated microbubbles destruction to treat colon cancer in a mouse model. Cancer Lett. 2013;335:183–190. [PubMed] [Google Scholar]
64. Hunt SJ, Gade T, Soulen MC, Pickup S, Sehgal CM. Antivascular ultrasound therapy: MR validation and activation of immune response in murine melanoma. J Ultrasound Med. 2014 (in press) [PubMed] [Google Scholar]
65. Husseini GA, Pitt WG. Ultrasonic-activated micellar drug delivery for cancer treatment. J Pharm Sci. 2009;98:795–811. [PMC free article] [PubMed] [Google Scholar]
66. Hyvelin JM, Tardy I, Arbogast C, Costa M, Emmel P, Helbert A, Theraulaz M, Nunn AD, Tranquart F. Use of ultrasound contrast agent microbubbles in preclinical research: recommendations for small animal imaging. Invest Radiol. 2013;48:570–583. [PubMed] [Google Scholar]
67. Ibsen S, Benchimol M, Simberg D, Esener S. Ultrasound mediated localized drug delivery. Adv Exp Med Biol. 2012;733:145–153. [PubMed] [Google Scholar]
68. Ibsen S, Schutt CE, Esener S. Microbubble-mediated ultrasound therapy: a review of its potential in cancer treatment. Drug Des Devel Ther. 2013;7:375–388. [PMC free article] [PubMed] [Google Scholar]
69. Jeong EJ, Seo SJ, Ahn YJ, Choi KH, Kim KH, Kim JK. Sonodynamically induced antitumor effects of 5-aminolevulinic acid and fractionated ultrasound irradiation in an orthotopic rat glioma model. Ultrasound Med Biol. 2012;38:2143–2150. [PubMed] [Google Scholar]
70. Jin ZH, Miyoshi N, Ishiguro K, Umemura S, Kawabata K, Yumita N, Sakata I, Takaoka K, Udagawa T, Nakajima S, Tajiri H, Ueda K, Fukuda M, Kumakiri M. Combination effect of photodynamic and sonodynamic therapy on experimental skin squamous cell carcinoma in C3H/HeN mice. J Dermatol. 2000;27:294–306. [PubMed] [Google Scholar]
71. Kang J, Wu X, Wang Z, Ran H, Xu C, Wu J, Wang Z, Zhang Y. Antitumor effect of docetaxel-loaded lipid microbubbles combined with ultrasound-targeted microbubble activation on VX2 rabbit liver tumors. J Ultrasound Med. 2010;29:61–70. [PubMed] [Google Scholar]
72. Kang ST, Yeh CK. Ultrasound microbubble contrast agents for diagnostic and therapeutic applications: current status and future design. Chang Gung Med J. 2012;35:125–139. [PubMed] [Google Scholar]
73. Kovacs Z, Werner B, Rassi A, Sass JO, Martin-Fiori E, Bernasconi M. Prolonged survival upon ultrasound-enhanced doxorubicin delivery in two syngenic glioblastoma mouse models. J Control Release. 2014;187:74–82. [PubMed] [Google Scholar]
74. Klotz AR, Lindvere L, Stefanovic B, Hynynen K. Temperature change near microbubbles within a capillary network during focused ultrasound. Phys Med Biol. 2010 Mar 21;55(6):1549–61. [PMC free article] [PubMed] [Google Scholar]
75. Kuroki M, Hachimine K, Abe H, Shibaguchi H, Kuroki M, Maekawa S, Yanagisawa J, Kinugasa T, Tanaka T, Yamashita Y. Sonodynamic therapy of cancer using novel sonosensitizers. Anticancer Res. 2007;27:3673–3677. [PubMed] [Google Scholar]
76. Lentacker I, Geers B, Demeester J, De Smedt SC, Sanders NN. Design and evaluation of doxorubicin-containing microbubbles for ultrasound-triggered doxorubicin delivery: cytotoxicity and mechanisms involved. Mol Ther. 2010;18:101–108. [PMC free article] [PubMed] [Google Scholar]
77. Levenback BJ, Sehgal CM, Wood AK. Modeling of thermal effects in antivascular ultrasound therapy. J Acoust Soc Am. 2012;131:540–549. [PMC free article] [PubMed] [Google Scholar]
78. Li H, Fan H, Wang Z, Zheng J, Cao W. Potentiation of scutellarin on human tongue carcinoma xenograft by low-intensity ultrasound. PLoS One. 2013;8:e59473. [PMC free article] [PubMed] [Google Scholar]
79. Li Y, Wang P, Zhao P, Zhu S, Wang X, Liu Q. Apoptosis induced by sonodynamic treatment by protoporphyrin IX on MDA-MB-231 cells. Ultrasonics. 2012[a];52:490–496. [PubMed] [Google Scholar]
80. Li P, Zheng Y, Ran H, Tan J, Lin Y, Zhang Q, Ren J, Wang Z. Ultrasound triggered drug release

from 10-hydroxycamptothecin-loaded phospholipid microbubbles for targeted tumor therapy in mice. J Control Release. 2012[b];162:349–354. [PubMed] [Google Scholar]
81. Li XH, Zhou P, Wang LH, Tian SM, Qian Y, Chen LR, Zhang P. The targeted gene (KDRP-CD/TK) therapy of breast cancer mediated by SonoVue and ultrasound irradiation in vitro. Ultrasonics. 2012[c];52:186–191. [PubMed] [Google Scholar]
82. Li F, Jin L, Wang H, Wei F, Bai M, Shi Q, Du L. The dual effect of ultrasound-targeted microbubble destruction in mediating recombinant adeno-associated virus delivery in renal cell carcinoma: transfection enhancement and tumor inhibition. J Gene Med. 2014;16:28–39. [PubMed] [Google Scholar]
83. Liang HD, Tang J, Halliwell M. Sonoporation, drug delivery, and gene therapy. Proc Inst Mech Eng H. 2010;224:343–361. [PubMed] [Google Scholar]
84. Liang L, Xie S, Jiang L, Jin H, Li S, Liu J. The Combined effects of hematoporphyrin monomethyl ether-SDT and doxorubicin on the proliferation of QBC939 cell lines. Ultrasound Med Biol. 2013;39:146–160. [PubMed] [Google Scholar]
85. Liao AH, Li YK, Lee WJ, Wu MF, Liu HL, Kuo ML. Estimating the delivery efficiency of drug-loaded microbubbles in cancer cells with ultrasound and bioluminescence imaging. Ultrasound Med Biol. 2012;38:1938–1948. [PubMed] [Google Scholar]
86. Liao AH, Liu HL, Su CH, Hua MY, Yang HW, Weng YT, Hsu PH, Huang SM, Wu SY, Wang HE, Yen TC, Li PC. Paramagnetic perfluorocarbon-filled albumin-(Gd-DTPA) microbubbles for the induction of focused-ultrasound-induced blood-brain barrier opening and concurrent MR and ultrasound imaging. Phys Med Biol. 2012;57:2787–2802. [PubMed] [Google Scholar]
87. Lim AK, Patel N, Eckersley RJ, Taylor-Robinson SD, Cosgrove DO, Blomley MJ. Evidence for spleen-specific uptake of a microbubble contrast agent: a quantitative study in healthy volunteers. Radiology. 2004;231:785–788. [PubMed] [Google Scholar]
88. Lin CY, Li JR, Tseng HC, Wu MF, Lin WL. Enhancement of focused ultrasound with microbubbles on the treatments of anticancer nanodrug in mouse tumors. Nanomedicine. 2012[a];8:900–907. [PubMed] [Google Scholar]
89. Lin CY, Tseng HC, Shiu HR, Wu MF, Chou CY, Lin WL. Ultrasound sonication with microbubbles disrupts blood vessels and enhances tumor treatments of anticancer nanodrug. Int J Nanomedicine. 2012[b];7:2143–2152. [PMC free article] [PubMed] [Google Scholar]
90. Lionetti V, Paddeu S. Paradossi G, Pellegretti P, Trucco A, editors. Towards ultrasound molecular imaging. Ultrasound contrast agents. Targeting and processing methods for theranostics. 2010:1. [Google Scholar]
91. Liu Y, Miyoshi H, Nakamura M. Encapsulated ultrasound microbubbles: therapeutic application in drug/gene delivery. J Control Release. 2006[a];114:89–99. [PubMed] [Google Scholar]
92. Liu Q, Wang X, Wang P, Qi H, Zhang K, Xiao L. Sonodynamic effects of protoporphyrin IX disodium salt on isolated sarcoma 180 cells. Ultrasonics. 2006[b];45:56–60. [PubMed] [Google Scholar]
93. Liu Q, Wang X, Wang P, Xiao L. Sonodynamic antitumor effect of protoporphyrin IX disodium salt on S180 solid tumor. Chemotherapy. 2007 (a);53:429–436. [PubMed] [Google Scholar]
94. Liu Q, Wang X, Wang P, Xiao L, Hao Q. Comparison between sonodynamic effect with protoporphyrin IX and hematoporphyrin on sarcoma 180. Cancer Chemother Pharmacol. 2007 (b);60:671–680. [PubMed] [Google Scholar]
95. Liu GJ, Moriyasu F, Hirokawa T, Rexiati M, Yamada M, Imai Y. Optical microscopic findings of the behavior of perflubutane microbubbles outside and insideKupffer cells during diagnostic ultrasound examination. Invest Radiol. 2008[a];43:829–836. [PubMed] [Google Scholar]
96. Liu Q, Li X, Xiao L, Wang P, Wang X, Tang W. Sonodynamically induced antitumor effect of hematoporphyrin on Hepatoma 22. Ultrason Sonochem. 2008[b];15:943–948. [PubMed] [Google Scholar]
97. Liu HL, Hua MY, Chen PY, Chu PC, Pan CH, Yang HW, Huang CY, Wang JJ, Yen TC, Wei KC. Blood-brain barrier disruption with focused ultrasound enhances delivery of chemotherapeutic drugs for glioblastoma treatment. Radiology. 2010;255:415–425. [PubMed] [Google Scholar]
98. Liu Z, Gao S, Zhao Y, Li P, Liu J, Li P, Tan K, Xie F. Disruption of tumor neovasculature by microbubble enhanced ultrasound: a potential new physical therapy of anti-angiogenesis. Ultrasound Med Biol. 2012;38:253–261. [PubMed] [Google Scholar]

99. Liu YN, Khangura J, Xie A, Belcik JT, Qi Y, Davidson BP, Zhao Y, Kim S, Inaba Y, Lindner JR. Renal retention of lipid microbubbles: a potential mechanism for flank discomfort during ultrasound contrast administration. J Am Soc Echocardiogr. 2013[a];26:1474–1481. [PMC free article] [PubMed] [Google Scholar]
100. Liu Q, Zhao H, Wu S, Zhao X, Zhong Y, Li L, Liu Z. Impact of microbubble-enhanced ultrasound on liver ethanol ablation. Ultrasound Med Biol. 2013[b];39:1039–1046. [PubMed] [Google Scholar]
101. Liu HL, Fan CH, Ting CY, Yeh CK. Combining microbubbles and ultrasound for drug delivery to brain tumors: current progress and overview. Theranostics. 2014;4:432–444. [PMC free article] [PubMed] [Google Scholar]
102. Lu CT, Zhao YZ, Wu Y, Tian XQ, Li WF, Huang PT, Li XK, Sun CZ, Zhang L. Experiment on enhancing antitumor effect of intravenous epirubicin hydrochloride by acoustic cavitation in situ combined with phospholipid-based microbubbles. Cancer Chemother Pharmacol. 2011;68:343–348. [PubMed] [Google Scholar]
103. Lv Y, Fang M, Zheng J, Yang B, Li H, Xiuzigao Z, Song W, Chen Y, Cao W. Low-intensity ultrasound combined with 5-aminolevulinic acid administration in the treatment of human tongue squamous carcinoma. Cell Physiol Biochem. 2012;30:321–333. [PubMed] [Google Scholar]
104. Mason RP, Zhao D, Liu L, Trawick ML, Pinney KG. A perspective on vascular disrupting agents that interact with tubulin: preclinical tumor imaging and biological assessment. Integr Biol (Camb) 2011;3:375–387. [PMC free article] [PubMed] [Google Scholar]
105. Matsuo M, Yamaguchi K, Feril LB, Jr, Endo H, Ogawa K, Tachibana K, Nakayama J. Synergistic inhibition of malignant melanoma proliferation by melphalan combined with ultrasound and microbubbles. Ultrason Sonochem. 2011;18:1218–1224. [PubMed] [Google Scholar]
106. Mayer CR, Geis NA, Katus HA, Bekeredjian R. Ultrasound targeted microbubble destruction for drug and gene delivery. Expert Opin Drug Deliv. 2008;5:1121–1138. [PubMed] [Google Scholar]
107. McDannold NJ, Vykhodtseva NI, Hynynen K. Microbubble contrast agent with focused ultrasound to create brain lesions at low power levels: MR imaging and histologic study in rabbits. Radiology. 2006;241:95–106. [PubMed] [Google Scholar]
108. Meijering BD, Juffermans LJ, van Wamel A, Henning RH, Zuhorn IS, Emmer M, Versteilen AM, Paulus WJ, van Gilst WH, Kooiman K, de Jong N, Musters RJ, Deelman LE, Kamp O. Ultrasound and microbubble-targeted delivery of macromolecules is regulated by induction of endocytosis and pore formation. Circ Res. 2009;104:679–687. [PubMed] [Google Scholar]
109. Misík V, Riesz P. Free radical intermediates in sonodynamic therapy. N Y Acad Sci. 2000;899:335–348. [PubMed] [Google Scholar]
110. Nie F, Xu HX, Lu MD, Wang Y, Tang Q. Anti-angiogenic gene therapy for hepatocellular carcinoma mediated by microbubble-enhanced ultrasound exposure: an in vivo experimental study. J Drug Target. 2008;16:389–395. [PubMed] [Google Scholar]
111. Ninomiya K, Ogino C, Oshima S, Sonoke S, Kuroda S, Shimizu N. Targeted sonodynamic therapy using protein-modified TiO2 nanoparticles. Ultrason Sonochem. 2012;19:607–614. [PubMed] [Google Scholar]
112. Ninomiya K, Noda K, Ogino C, Kuroda S, Shimizu N. Enhanced OH radical generation by dual-frequency ultrasound with TiO2 nanoparticles: its application to targeted sonodynamic therapy. Ultrason Sonochem. 2014;21:289–294. [PubMed] [Google Scholar]
113. Niu C, Wang Z, Lu G, Krupka TM, Sun Y, You Y, Song W, Ran H, Li P, Zheng Y. Doxorubicin loaded superparamagnetic PLGA-iron oxide multifunctional microbubbles for dual-mode US/MR imaging and therapy of metastasis in lymph nodes. Biomaterials. 2013;34:2307–2317. [PubMed] [Google Scholar]
114. Nomikou N, Li YS, McHale AP. Ultrasound-enhanced drug dispersion through solid tumours and its possible role in aiding ultrasound-targeted cancer chemotherapy. Cancer Lett. 2010[a];288:94–98. [PubMed] [Google Scholar]
115. Nomikou N, McHale AP. Exploiting ultrasound-mediated effects in delivering targeted, site-specific cancer therapy. Cancer Lett. 2010[b];296:133–143. [PubMed] [Google Scholar]
116. Ohmura T, Fukushima T, Shibaguchi H, Yoshizawa S, Inoue T, Kuroki M, Sasaki K, Umemura S. Sonodynamic therapy with 5-aminolevulinic acid and focused ultrasound for deep-seated intracranial glioma in rat. Anticancer Res. 2011;31:2527–2533. [PubMed] [Google Scholar]
117. Owen J, Pankhurst Q, Stride E. Magnetic targeting and ultrasound mediated drug delivery: benefits, limitations and combination. Int J Hyperthermia. 2012;28:362–373. [PubMed] [Google Scholar]

118. Park EJ, Zhang YZ, Vykhodtseva N, McDannold N. Ultrasound-mediated blood-brain/blood-tumor barrier disruption improves outcomes with trastuzumab in a breast cancer brain metastasis model. J Control Release. 2012;163:277–284. [PMC free article] [PubMed] [Google Scholar]
119. Peijing L, Mei Z, Yali X, Yang Z, Shunji G, Gao Yun-hua G. Impact of microbubble enhanced, pulsed, focused ultrasound on tumor circulation of subcutaneous VX2 cancer. Chinese Medical Journal. 2014;127:2605–2611. [PubMed] [Google Scholar]
120. Perini R, Choe R, Yodh AG, Sehgal C, Divgi CR, Rosen MA. Non-invasive assessment of tumor neovasculature: techniques and clinical applications. Cancer Metastasis Rev. 2008;27:615–630. [PubMed] [Google Scholar]
121. Peyman SA, Abou-Saleh RH, Evans SD. Research Spotlight: Microbubbles for therapeutic delivery. Ther Deliv. 2013;4:539–542. [PubMed] [Google Scholar]
122. Preston RC. Hydrophone-based measurements on a specific acoustic pulse. Part 1: Field characterization. In: Preston RC, editor. Output measurements for medical ultrasound. Springer-Verlag; London, UK: 1991. p. 95. [Google Scholar]
123. Rapoport N. Ultrasound-mediated micellar drug delivery. Int J Hyperthermia. 2012;28:374–385. [PubMed] [Google Scholar]
124. Rapoport N, Gao Z, Kennedy A. Multifunctional nanoparticles for combining ultrasonic tumor imaging and targeted chemotherapy. J Natl Cancer Inst. 2007;99:1095–2152. [PubMed] [Google Scholar]
125. Rapoport NY, Kennedy AM, Shea JE, Scaife CL, Nam KH. Controlled and targeted tumor chemotherapy by ultrasound-activated nanoemulsions/microbubbles. J Control Release. 2009;138:268–276. [PMC free article] [PubMed] [Google Scholar]
126. Razansky D, Einziger PD, Adam DR. Enhanced heat deposition using ultrasound contrast agent--modeling and experimental observations. IEEE Trans Ultrason Ferroelectr Freq Control. 2006;53:137–147. [PubMed] [Google Scholar]
127. Ren ST, Liao YR, Kang XN, Li YP, Zhang H, Ai H, Sun Q, Jing J, Zhao XH, Tan LF, Shen XL, Wang B. The antitumor effect of a new docetaxel-loaded microbubble combined with low-frequency ultrasound in vitro: preparation and parameter analysis. Pharm Res. 2013 Feb;:16. [Epub ahead of print] [PubMed] [Google Scholar]
128. Rosenthal I, Sostaric JZ, Riesz P. Sonodynamic therapy--a review of the synergistic effects of drugs and ultrasound. Ultrason Sonochem. 2004;11:349–363. [PubMed] [Google Scholar]
129. Sakakima Y, Hayashi S, Yagi Y, Hayakawa A, Tachibana K, Nakao A. Gene therapy for hepatocellular carcinoma using sonoporation enhanced by contrast agents. Cancer Gene Ther. 2005;12:884–889. [PubMed] [Google Scholar]
130. Samiotaki G, Konofagou EE. Dependence of the reversibility of focused-ultrasound-induced blood-brain barrier opening on pressure and pulse length in vivo. IEEE Trans Ultrason Ferroelectr Freq Control. 2013;60:2257–2265. [PMC free article] [PubMed] [Google Scholar]
131. Sazgarnia A, Shanei A, Meibodi NT, Eshghi H, Nassirli H. A novel nanosonosensitizer for sonodynamic therapy: in vivo study on a colon tumor model. J Ultrasound Med. 2011;30:1321–1329. [PubMed] [Google Scholar]
132. Schroeder A, Honen R, Turjeman K, Gabizon A, Kost J, Barenholz Y. Ultrasound triggered release of cisplatin from liposomes in murine tumors. J Control Release. 2009[a];137:63–8. [PubMed] [Google Scholar]
133. Schroeder A, Kost J, Barenholz Y. Ultrasound, liposomes, and drug delivery: principles for using ultrasound to control the release of drugs from liposomes. Chem Phys Lipids. 2009[b];162:1–16. [PubMed] [Google Scholar]
134. Sehgal CM, Cary TW, Arger PH, Wood AKW. Delta-projection imaging on contrast-enhanced ultrasound to quantify tumor microvasculature and perfusion. Acad Radiol. 2009;16:71–78. [PMC free article] [PubMed] [Google Scholar]
135. Shanei A, Sazgarnia A, Tayyebi Meibodi N, Eshghi H, Hassanzadeh-Khayyat M, Esmaily H, Attaran Kakhki N. Sonodynamic Therapy Using Protoporphyrin IX Conjugated to Gold Nanoparticles: An In Vivo Study on a Colon Tumor Model. Iran J Basic Med Sci. 2012;15:759–767. [PMC free article] [PubMed] [Google Scholar]
136. Shi H, Liu Q, Qin X, Wang P, Wang X. Pharmacokinetic study of a novel sonosensitizer chlorin-e6 and its sonodynamic anti-cancer activity in hepatoma-22 tumor-bearing mice. Biopharm Drug Dispos. 2011;32:319–332. [PubMed] [Google Scholar]
137. Shibaguchi H, Tsuru H, Kuroki M, Kuroki M. Sonodynamic cancer therapy: a non-invasive and repeatable approach using low-intensity ultrasound with a sonosensitizer. Anticancer Res. 2011;31:2425–2429. [PubMed] [Google Scholar]
138. Siemannn DW. Tumor vasculature: a target for anticancer therapies. Vascular-targeted therapies in oncology. In: Siemann DW, editor. John Wiley

and Sons Ltd; Chichester: 2006. pp. 1–8. [Google Scholar]
139. Sirsi SR, Borden MA. Advances in ultrasound mediated gene therapy using microbubble contrast agents. Theranostics. 2012;2:1208–1222. [PMC free article] [PubMed] [Google Scholar]
140. Sirsi SR, Hernandez SL, Zielinski L, Blomback H, Koubaa A, Synder M, Homma S, Kandel JJ, Yamashiro DJ, Borden MA. Polyplex-microbubble hybrids for ultrasound-guided plasmid DNA delivery to solid tumors. J Control Release. 2012;157:224–234. [PMC free article] [PubMed] [Google Scholar]
141. Sorace AG, Warram JM, Umphrey H, Hoyt K. Microbubble-mediated ultrasonic techniques for improved chemotherapeutic delivery in cancer. J Drug Target. 2012;20:43–54. [PMC free article] [PubMed] [Google Scholar]
142. Staples BJ, Pitt WG, Roeder BL, Husseini GA, Rajeev D, Schaalje GB. Distribution of doxorubicin in rats undergoing ultrasonic drug delivery. J Pharm Sci. 2010;99:3122–3131. [PMC free article] [PubMed] [Google Scholar]
143. Stride EP, Coussios CC. Cavitation and contrast: the use of bubbles in ultrasound imaging and therapy. Proc Inst Mech Eng H. 2010;224:171–191. [PubMed] [Google Scholar]
144. Su X, Wang P, Wang X, Cao B, Li L, Liu Q. Apoptosis of U937 cells induced by hematoporphyrin monomethyl ether-mediated sonodynamic action. Cancer Biother Radiopharm. 2013[a];28:207–217. [PMC free article] [PubMed] [Google Scholar]
145. Su X, Wang P, Wang X, Guo L, Li S, Liu Q. Involvement of MAPK activation and ROS generation in human leukemia U937 cells undergoing apoptosis in response to sonodynamic therapy. Int J Radiat Biol. 2013[b];89:915–927. [PubMed] [Google Scholar]
146. Su X, Li Y, Wang P, Wang X, Liu Q. Protoporphyrin IX-mediated sonodynamic action induces apoptosis of K562 cells. Ultrasonics. 2014;54:275–284. [PubMed] [Google Scholar]
147. Sugita N, Iwase Y, Yumita N, Ikeda T, Umemura S. Sonodynamically induced cell damage using rose bengal derivative. Anticancer Res. 2010;30:3361–3366. [PubMed] [Google Scholar]
148. Tang W, Liu Q, Wang X, Mi N, Wang P, Zhang J. Membrane fluidity altering and enzyme inactivating in sarcoma 180 cells post the exposure to sonoactivated hematoporphyrin in vitro. Ultrasonics. 2008 [a];48:66–73. [PubMed] [Google Scholar]
149. Tang W, Liu Q, Wang X, Wang P, Cao B, Mi N, Zhang J. Involvement of caspase 8 in apoptosis induced by ultrasound-activated hematoporphyrin in sarcoma 180 cells in vitro. J Ultrasound Med. 2008 [b];27:645–656. [PubMed] [Google Scholar]
150. Tang W, Liu Q, Wang X, Zhang J, Wang P, Mi N. Ultrasound exposure in the presence of hematoporphyrin induced loss of membrane integral proteins and inactivity of cell proliferation associated enzymes in sarcoma 180 cells in vitro. Ultrason Sonochem. 2008 [c];15:747–754. [PubMed] [Google Scholar]
151. Tang Q, He X, Liao H, He L, Wang Y, Zhou D, Ye S, Chen Q. Ultrasound microbubble contrast agent-mediated suicide gene transfection in the treatment of hepatic cancer. Oncol Lett. 2012;4:970–972. [PMC free article] [PubMed] [Google Scholar]
152. Tian Z, Quan X, Xu C, Dan L, Guo H, Leung W. Hematoporphyrin monomethyl ether enhances the killing action of ultrasound on osteosarcoma in vivo. J Ultrasound Med. 2009;28:1695–1702. [PubMed] [Google Scholar]
153. Ting CY, Fan CH, Liu HL, Huang CY, Hsieh HY, Yen TC, Wei KC, Yeh CK. Concurrent blood-brain barrier opening and local drug delivery using drug-carrying microbubbles and focused ultrasound for brain glioma treatment. Biomaterials. 2012;33:704–712. [PubMed] [Google Scholar]
154. Tinkov S, Bekeredjian R, Winter G, Coester C. Microbubbles as ultrasound triggered drug carriers. J Pharm Sci. 2009;98:1935–1961. [PubMed] [Google Scholar]
155. Tinkov S, Coester C, Serba S, Geis NA, Katus HA, Winter G, Bekeredjian R. New doxorubicin-loaded phospholipid microbubbles for targeted tumor therapy: in-vivo characterization. J Control Release. 2010[a];148:368–372. [PubMed] [Google Scholar]
156. Tinkov S, Winter G, Coester C, Bekeredjian R. New doxorubicin-loaded phospholipid microbubbles for targeted tumor therapy: Part I--Formulation development and in-vitro characterization. J Control Release. 2010[b];143:143–150. [PubMed] [Google Scholar]
157. Todorova M, Agache V, Mortazavi O, Chen B, Karshafian R, Hynynen K, Man S, Kerbel RS, Goertz DE. Antitumor effects of combining metronomic chemotherapy with the antivascular action of ultrasound stimulated microbubbles. Int J Cancer. 2013;132:2956–2966. [PubMed] [Google Scholar]
158. Toft KG, Hustvedt SO, Hals PA, Oulie I, Uran S, Landmark K, Normann PT, Skotland T.

Disposition of perfluorobutane in rats after intravenous injection of Sonazoid. Ultrasound Med Biol. 2006;32:107–114. [PubMed] [Google Scholar]
159. Tomizawa M, Ebara M, Saisho H, Sakiyama S, Tagawa M. Irradiation with ultrasound of low output intensity increased chemosensitivity of subcutaneous solid tumors to an anti-cancer agent. Cancer Lett. 2001;173:31–35. [PubMed] [Google Scholar]
160. Treat LH, McDannold N, Zhang Y, Vykhodtseva N, Hynynen K. Improved anti-tumor effect of liposomal doxorubicin after targeted blood-brain barrier disruption by MRI-guided focused ultrasound in rat glioma. Ultrasound Med Biol. 2012;38:1716–1725. [PMC free article] [PubMed] [Google Scholar]
161. Trendowski M. The promise of sonodynamic therapy. Cancer Metastasis Rev. 2013 Dec;:18. [Epub ahead of print] [PubMed] [Google Scholar]
162. Tserkovsky DA, Alexandrova EN, Chalau VN, Istomin YP. Effects of combined sonodynamic and photodynamic therapies with photolon on a glioma C6 tumor model. Exp Oncol. 2012;34:332–335. [PubMed] [Google Scholar]
163. Tsuru H, Shibaguchi H, Kuroki M, Yamashita Y, Kuroki M. Tumor growth inhibition by sonodynamic therapy using a novel sonosensitizer. Free Radic Biol Med. 2012;53:464–472. [PubMed] [Google Scholar]
164. Tu J, Hwang JH, Matula TJ, Brayman AA, Crum LA. Intravascular inertial cavitation activity detection and quantification in vivo with Optison. Ultrasound Med Biol. 2006;32:1601–1609. [PubMed] [Google Scholar]
165. Umemura S, Yumita N, Nishigaki R, Umemura K. Mechanism of cell damage by ultrasound in combination with hematoporphyrin. Jpn J Cancer Res. 1990;81:962–966. [PMC free article] [PubMed] [Google Scholar]
166. Umemura S, Kawabata K, Sasaki K, Yumita N, Umemura K, Nishigaki R. Recent advances in sonodynamic approach to cancer therapy. Ultrason Sonochem. 1996 [a];3:S187–S191. [Google Scholar]
167. Umemura K, Yumita N, Nishigaki R, Umemura S. Sonodynamically induced antitumor effect of pheophorbide a. Cancer Lett. 1996[b];102:151–157. [PubMed] [Google Scholar]
168. Umemura S, Kawabata K, Sasaki K. In vivo acceleration of ultrasonic tissue heating by microbubble agent. IEEE Trans Ultrason Ferroelectr Freq Control. 2005;52:1690–1698. [PubMed] [Google Scholar]
169. Van Leenders GJLH, Beerlage HP, Th Ruijter E, de la Rosette JJMCH, van de Kaa CA. Histopathological changes associated with high intensity focused ultrasound (HIFU) treatment for localised adenocarcinoma of the prostate. J Clin Pathol. 2000;53:391–394. [PMC free article] [PubMed] [Google Scholar]
170. Vaupel P. Abnormal microvasculature and defective microcirculatory function in solid tumors. In: Siemann DW, editor. Vascular-targeted therapies in oncology. John Wiley and Sons Ltd; Chichester: 2006. pp. 9–29. [Google Scholar]
171. Verrall RE, Sehgal CM. Sonoluminescence. In: Suslick KS, editor. Utrasound. Its chemical, physical and biological effects. VCH Publishers Inc; New York: 1988. pp. 227–286. [Google Scholar]
172. Wang P, Wang XB, Liu QH, Tang W, Li T. Enhancement of ultrasonically induced cytotoxic effect by hematoporphyrin in vitro. Chemotherapy. 2008 [a];54:364–371. [PubMed] [Google Scholar]
173. Wang XB, Liu QH, Wang P, Tang W, Hao Q. Study of cell killing effect on S180 by ultrasound activating protoporphyrin IX. Ultrasonics. 2008 [b];48:135–140. [PubMed] [Google Scholar]
174. Wang XB, Liu QH, Wang P, Zhang K, Tang W, Wang BL. Enhancement of apoptosis by sonodynamic therapy with protoporphyrin IX in isolate sarcoma 180 cells. Cancer Biother Radiopharm. 2008 [c];23:238–246. [PubMed] [Google Scholar]
175. Wang X, Liu Q, Wang Z, Wang P, Zhao P, Zhao X, Yang L, Li Y. Role of autophagy in sonodynamic therapy-induced cytotoxicity in S180 cells. Ultrasound Med Biol. 2010;36:1933–46. [PubMed] [Google Scholar]
176. Wang X, Wang Y, Wang P, Cheng X, Liu Q. Sonodynamically induced anti-tumor effect with protoporphyrin IX on hepatoma-22 solid tumor. Ultrasonics. 2011 [a];51:539–546. [PubMed] [Google Scholar]
177. Wang X, Xia X, Leung AW, Xiang J, Jiang Y, Wang P, Xu J, Yu H, Bai D, Xu C. Ultrasound induces cellular destruction of nasopharyngeal carcinoma cells in the presence of curcumin. Ultrasonics. 2011 [b];51:165–170. [PubMed] [Google Scholar]
178. Wang X, Xia X, Xu C, Xu J, Wang P, Xiang J, Bai D, Leung AW. Ultrasound-induced cell death of nasopharyngeal carcinoma cells in the presence of curcumin. Integr Cancer Ther. 2011 [c];10:70–76. [PubMed] [Google Scholar]

179. Wang X, Leung AW, Jiang Y, Yu H, Li X, Xu C. Hypocrellin B-mediated sonodynamic action induces apoptosis of hepatocellular carcinoma cells. Ultrasonics. 2012 [a];52:543–546. [PubMed] [Google Scholar]
180. Wang X, Leung AW, Luo J, Xu C. TEM observation of ultrasound-induced mitophagy in nasopharyngeal carcinoma cells in the presence of curcumin. Exp Ther Med. 2012 [b];3:146–148. [PMC free article] [PubMed] [Google Scholar]
181. Wang DS, Panje C, Pysz MA, Paulmurugan R, Rosenberg J, Gambhir SS, Schneider M, Willmann JK. Cationic versus neutral microbubbles for ultrasound-mediated gene delivery in cancer. Radiology. 2012[c];264:721–732. [PMC free article] [PubMed] [Google Scholar]
182. Wang H, Liu Q, Zhang K, Wang P, Xue Q, Li L, Wang X. Comparison between sonodynamic and photodynamic effect on MDA-MB-231 cells. J Photochem Photobiol B. 2013[a];127:182–191. [PubMed] [Google Scholar]
183. Wang X, Wang P, Zhang K, Su X, Hou J, Liu Q. Initiation of autophagy and apoptosis by sonodynamic therapy in murine leukemia L1210 cells. Toxicol In Vitro. 2013[b];27:1247–1259. [PubMed] [Google Scholar]
184. Wang G, Zhuo Z, Xia H, Zhang Y, He Y, Tan W, Gao Y. Investigation into the impact of diagnostic ultrasound with microbubbles on the capillary permeability of rat hepatomas. Ultrasound Med Biol. 2013[c];39:628–637. [PubMed] [Google Scholar]
185. Watanabe Y, Aoi A, Horie S, Tomita N, Mori S, Morikawa H, Matsumura Y, Vassaux G, Kodama T. Low-intensity ultrasound and microbubbles enhance the antitumor effect of cisplatin. Cancer Sci. 2008;99:2525–2531. [PubMed] [Google Scholar]
186. Wei KC, Chu PC, Wang HY, Huang CY, Chen PY, Tsai HC, Lu YJ, Lee PY, Tseng IC, Feng LY, Hsu PW, Yen TC, Liu HL. Focused ultrasound-induced blood-brain barrier opening to enhance temozolomide delivery for glioblastoma treatment: a preclinical study. PLoS One. 2013;8:e58995. [PMC free article] [PubMed] [Google Scholar]
187. Wood AK, Ansaloni S, Ziemer LS, Lee WM, Feldman MD, Sehgal CM. The antivascular action of physiotherapy ultrasound on murine tumors. Ultrasound Med Biol. 2005;31:1403–1410. [PMC free article] [PubMed] [Google Scholar]
188. Wood AK, Bunte RM, Ansaloni S, Lee WM, Sehgal CM. The antivascular actions of mild intensity ultrasound on a murine neoplasm. In: Clement GT, McDannold NJ, Hynynen K, editors. Therapeutic ultrasound: 5th International Symposium on Therapeutic Ultrasound.2006. pp. 467–470. [Google Scholar]
189. Wood AK, Bunte RM, Cohen JD, Tsai JH, Lee WM, Sehgal CM. The antivascular action of physiotherapy ultrasound on a murine tumor: role of a microbubble contrast agent. Ultrasound Med Biol. 2007;33:1901–1910. [PMC free article] [PubMed] [Google Scholar]
190. Wood AK, Bunte RM, Price HE, Deitz MS, Tsai JH, Lee WM, Sehgal CM. The disruption of murine tumor neovasculature by low-intensity ultrasound-comparison between 1- and 3-MHz sonication frequencies. Acad Radiol. 2008;15:1133–1141. [PMC free article] [PubMed] [Google Scholar]
191. Wood AK, Bunte RM, Schultz SM, Sehgal CM. Acute increases in murine tumor echogenicity after antivascular ultrasound therapy: a pilot preclinical study. J Ultrasound Med. 2009;28:795–800. [PubMed] [Google Scholar]
192. Wood AK, Schultz SM, Lee WM, Bunte RM, Sehgal CM. Antivascular ultrasound therapy extends survival of mice with implanted melanomas. Ultrasound Med Biol. 2010;36:853–857. [PMC free article] [PubMed] [Google Scholar]
193. Wu F, Chen WZ, Bai J, Zou JZ, Wang ZL, Zhu H, Wang ZB. Pathological changes in human malignant carcinoma treated with high intensity focused ultrasound. Ultrasound Med Biol. 2001;27:1099–1106. [PubMed] [Google Scholar]
194. Wu F, Chen W-Z, Bai J, Zou JZ, Wang ZL, Zhu H, Wang ZB. Tumor vessel disruption resulting from high-intensity focused ultrasound in patients with solid malignancies. Ultrasound Med Biol. 2002;28:535–542. [PubMed] [Google Scholar]
195. Xiang J, Xia X, Jiang Y, Leung AW, Wang X, Xu J, Wang P, Yu H, Bai D, Xu C. Apoptosis of ovarian cancer cells induced by methylene blue-mediated sonodynamic action. Ultrasonics. 2011;51:390–395. [PubMed] [Google Scholar]
196. Xu ZY, Li XQ, Chen S, Cheng Y, Deng JM, Wang ZG. Glioma stem-like cells are less susceptible than glioma cells to sonodynamic therapy with photofrin. Technol Cancer Res Treat. 2012;11:615–623. [PubMed] [Google Scholar]
197. Xu ZY, Wang K, Li XQ, Chen S, Deng JM, Cheng Y, Wang ZG. The ABCG2 transporter is a key molecular determinant of the efficacy of sonodynamic therapy with Photofrin in glioma

stem-like cells. Ultrasonics. 2013;53:232–238. [PubMed] [Google Scholar]
198. Yamaguchi K, Feril LB, Jr, Tachibana K, Takahashi A, Matsuo M, Endo H, Harada Y, Nakayama J. Ultrasound-mediated interferon β gene transfection inhibits growth of malignant melanoma. Biochem Biophys Res Commun. 2011[a];411:137–142. [PubMed] [Google Scholar]
199. Yamaguchi S, Kobayashi H, Narita T, Kanehira K, Sonezaki S, Kudo N, Kubota Y, Terasaka S, Houkin K. Sonodynamic therapy using water-dispersed TiO2-polyethylene glycol compound on glioma cells: comparison of cytotoxic mechanism with photodynamic therapy. Ultrason Sonochem. 2011[b];18:1197–1204. [PubMed] [Google Scholar]
200. Yan F, Li L, Deng Z, Jin Q, Chen J, Yang W, Yeh CK, Wu J, Shandas R, Liu X, Zheng H. Paclitaxel-liposome-microbubble complexes as ultrasound-triggered therapeutic drug delivery carriers. J Control Release. 2013;166:246–255. [PubMed] [Google Scholar]
201. Yan F, Li X, Jin Q, Jiang C, Zhang Z, Ling T, Qiu B, Zheng H. Therapeutic ultrasonic microbubbles carrying paclitaxel and LyP-1 peptide: preparation, characterization and application to ultrasound-assisted chemotherapy in breast cancer cells. Ultrasound Med Biol. 2011;37:768–779. [PubMed] [Google Scholar]
202. Yanagisawa K, Moriyasu F, Miyahara T, Yuki M, Iijima H. Phagocytosis of ultrasound contrast agent microbubbles by Kupffer cells. Ultrasound Med Biol. 2007;33:318–325. [PubMed] [Google Scholar]
203. Yang S, Wang P, Wang X, Su X, Liu Q. Activation of microbubbles by low-level therapeutic ultrasound enhances the antitumor effects of doxorubicin. Eur Radiol. 2014 Aug;:6. [Epub ahead of print] [PubMed] [Google Scholar]
204. Yoshida T, Kondo T, Ogawa R, Feril LB, Jr, Zhao QL, Watanabe A, Tsukada K. Combination of doxorubicin and low-intensity ultrasound causes a synergistic enhancement in cell killing and an additive enhancement in apoptosis induction in human lymphoma U937 cells. Cancer Chemother Pharmacol. 2008;61:559–567. [PubMed] [Google Scholar]
205. Yu T, Bai J, Hu K, Wang Z. Biological effects of ultrasound exposure on adriamycin-resistant and cisplatin-resistant human ovarian carcinoma cell lines in vitro. Ultrason Sonochem. 2004[a];11:89–94. [PubMed] [Google Scholar]
206. Yu T, Huang X, Hu K, Bai J, Wang Z. Treatment of transplanted adriamycin-resistant ovarian cancers in mice by combination of adriamycin and ultrasound exposure. Ultrason Sonochem. 2004[b];11:287–291. [PubMed] [Google Scholar]
207. Yu T, Wang Z, Mason TJ. A review of research into the uses of low level ultrasound in cancer therapy. Ultrason Sonochem. 2004[c];11:95–103. [PubMed] [Google Scholar]
208. Yu BF, Wu J, Zhang Y, Sung HW, Xie J, Li RK. Ultrasound-targeted HSVtk and Timp3 gene delivery for synergistically enhanced antitumor effects in hepatoma. Cancer Gene Ther. 2013;20:290–297. [PubMed] [Google Scholar]
209. Yumita N, Nishigaki R, Umemura K, Umemura S. Hematoporphyrin as a sensitizer of cell-damaging effect of ultrasound. Jpn J Cancer Res. 1989;80:219–222. [PMC free article] [PubMed] [Google Scholar]
210. Yumita N, Nishigaki R, Umemura K, Umemura S. Synergistic effect of ultrasound and hematoporphyrin on sarcoma 180. Jpn J Cancer Res. 1990;81:304–308. [PMC free article] [PubMed] [Google Scholar]
211. Yumita N, Nishigaki R, Sakata I, Nakajima S, Umemura S. Sonodynamically induced antitumor effect of 4-formyloximethylidene-3-hydroxy-2-vinyl-deuterio-porphynyl(IX)-6,7-dia spartic acid (ATX-S10) Jpn J Cancer Res. 2000 [a];91:255–60. [PMC free article] [PubMed] [Google Scholar]
212. Yumita N, Nishigaki R, Umemura S. Sonodynamically induced antitumor effect of Photofrin II on colon 26 carcinoma. J Cancer Res Clin Oncol. 2000 [b];126:601–606. [PubMed] [Google Scholar]
213. Yumita N, Umemura S, Nishigaki R. Ultrasonically induced cell damage enhanced by photofrin II: mechanism of sonodynamic activation. In Vivo. 2000 [c];14:425–429. [PubMed] [Google Scholar]
214. Yumita N, Iwase Y, Nishi K, Ikeda T, Umemura S, Sakata I, Momose Y. Sonodynamically induced cell damage and membrane lipid peroxidation by novel porphyrin derivative, DCPH-P-Na(I) Anticancer Res. 2010;30:2241–2246. [PubMed] [Google Scholar]
215. Yumita N, Iwase Y, Nishi K, Ikeda T, Komatsu H, Fukai T, Onodera K, Nishi H, Takeda K, Umemura S, Okudaira K, Momose Y. Sonodynamically-induced antitumor effect of mono-l-aspartyl chlorin e6 (NPe6) Anticancer Res. 2011;31:501–506. [PubMed] [Google Scholar]
216. Yumita N, Iwase Y, Imaizumi T, Sakurazawa A, Kaya Y, Nishi K, Ikeda T, Umemura S, Chen FS, Momose Y. Sonodynamically-induced anticancer

effects by functionalized fullerenes. Anticancer Res. 2013;33:3145–3151. [PubMed] [Google Scholar]

217. Zhang X, Li K, Cui X, Hu L, Chen Y. Combined pluronic P85- and ultrasound contrast agents-mediated gene transfection to HepG2 cells. J Huazhong Univ Sci Technolog Med Sci. 2011;31:842–845. [PubMed] [Google Scholar]
218. Zhang C, Huang P, Zhang Y, Chen J, Shentu W, Sun Y, Yang Z, Chen S. Anti-tumor efficacy of ultrasonic cavitation is potentiated by concurrent delivery of anti-angiogenic drug in colon cancer. Cancer Lett. 2014;347:105–1013. [PubMed] [Google Scholar]
219. Zhao YZ, Dai DD, Lu CT, Lv HF, Zhang Y, Li X, Li WF, Wu Y, Jiang L, Li XK, Huang PT, Chen LJ, Lin M. Using acoustic cavitation to enhance chemotherapy of DOX liposomes: experiment in vitro and in vivo. Drug Dev Ind Pharm. 2012;38:1090–1098. [PubMed] [Google Scholar]
220. Zhao YZ, Du LN, Lu CT, Jin YG, Ge SP. Potential and problems in ultrasound-responsive drug delivery systems. Int J Nanomedicine. 2013;8:1621–1633. [PMC free article] [PubMed] [Google Scholar]
221. Zhao X, Liu Q, Tang W, Wang X, Wang P, Gong L, Wang Y. Damage effects of protoporphyrin IX - sonodynamic therapy on the cytoskeletal F-actin of Ehrlich ascites carcinoma cells. Ultrason Sonochem. 2009;16:50–56. [PubMed] [Google Scholar]
222. Zheng Y, Zhang Y, Ao M, Zhang P, Zhang H, Li P, Qing L, Wang Z, Ran H. Hematoporphyrin encapsulated PLGA microbubble for contrast enhanced ultrasound imaging and sonodynamic therapy. J Microencapsul. 2012;29:437–444. [PubMed] [Google Scholar]
223. Zhong H, Li R, Hao YX, Guo YL, Hua X, Zhang XH, Chen ZH. Inhibition effects of high mechanical index ultrasound contrast on hepatic metastasis of cancer in a rat model. Acad Radiol. 2010;17:1345–1349. [PubMed] [Google Scholar]
224. Zhou S, Li S, Liu Z, Tang Y, Wang Z, Gong J, Liu C. Ultrasound-targeted microbubble destruction mediated herpes simplex virus-thymidine kinase gene treats hepatoma in mice. J Exp Clin Cancer Res. 2010 Dec 23;29:170. (pages 1-6) [PMC free article] [PubMed] [Google Scholar]
225. Zolochevska O, Xia X, Williams BJ, Ramsay A, Li S, Figueiredo ML. Sonoporation delivery of interleukin-27 gene therapy efficiently reduces prostate tumor cell growth in vivo. Hum Gene Ther. 2011;22:1537–1550. [PMC free article] [PubMed] [Google Scholar]