Chap. 9
Emerging Therapeutic Ultrasound

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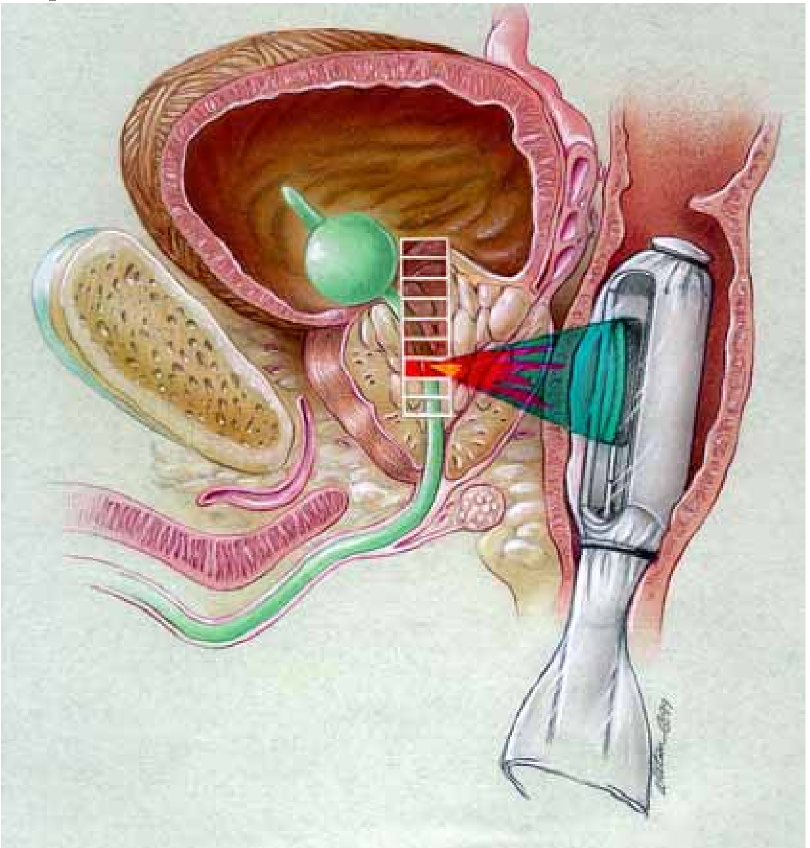
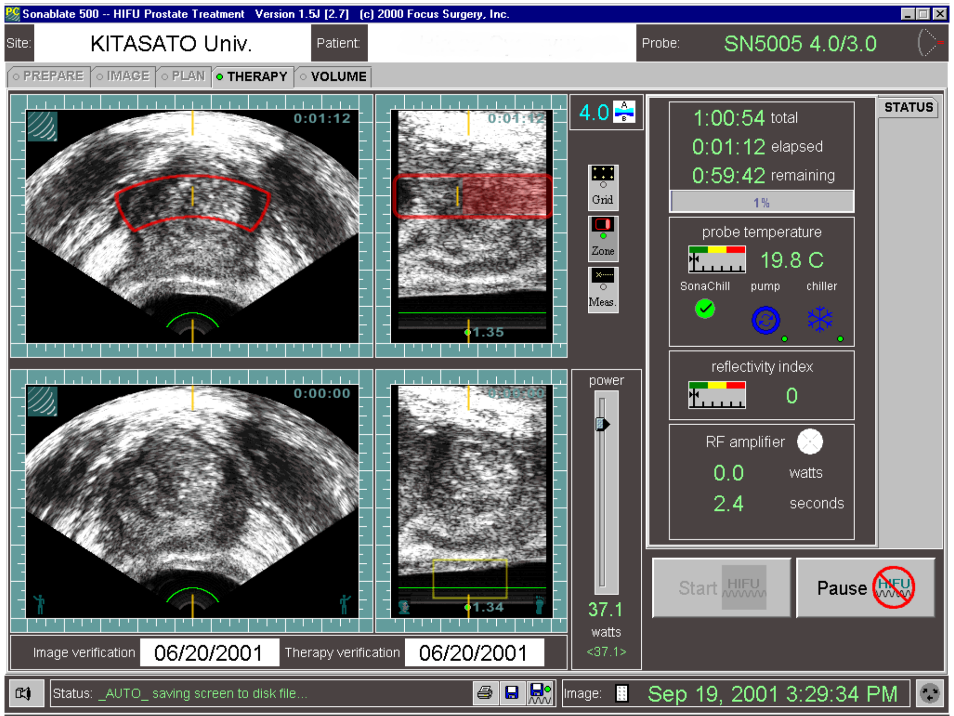
Focused ultrasound treatment of prostate hyperplasia and prostate cancer

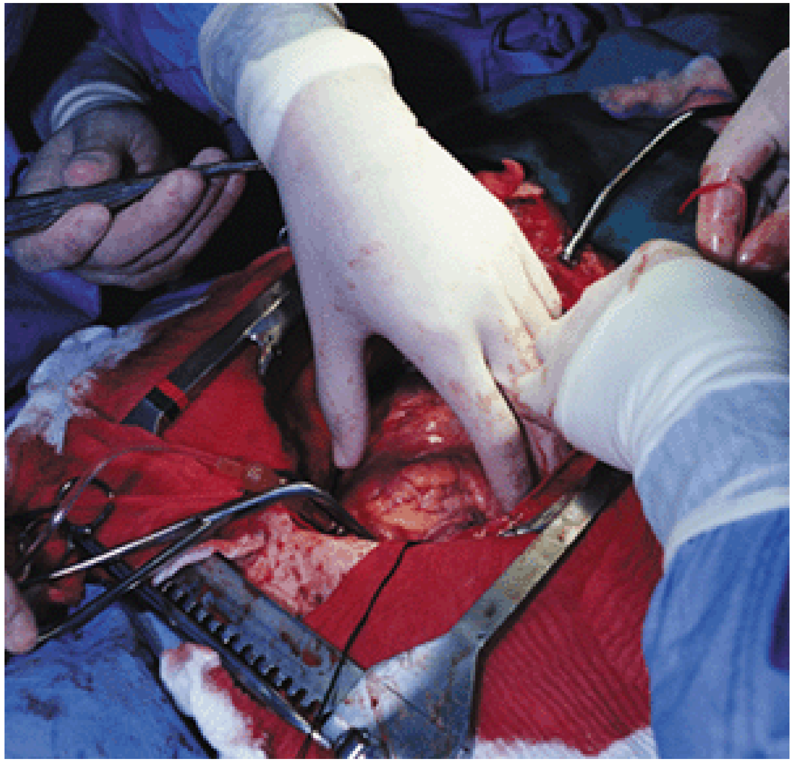




Transurethra and transrecta

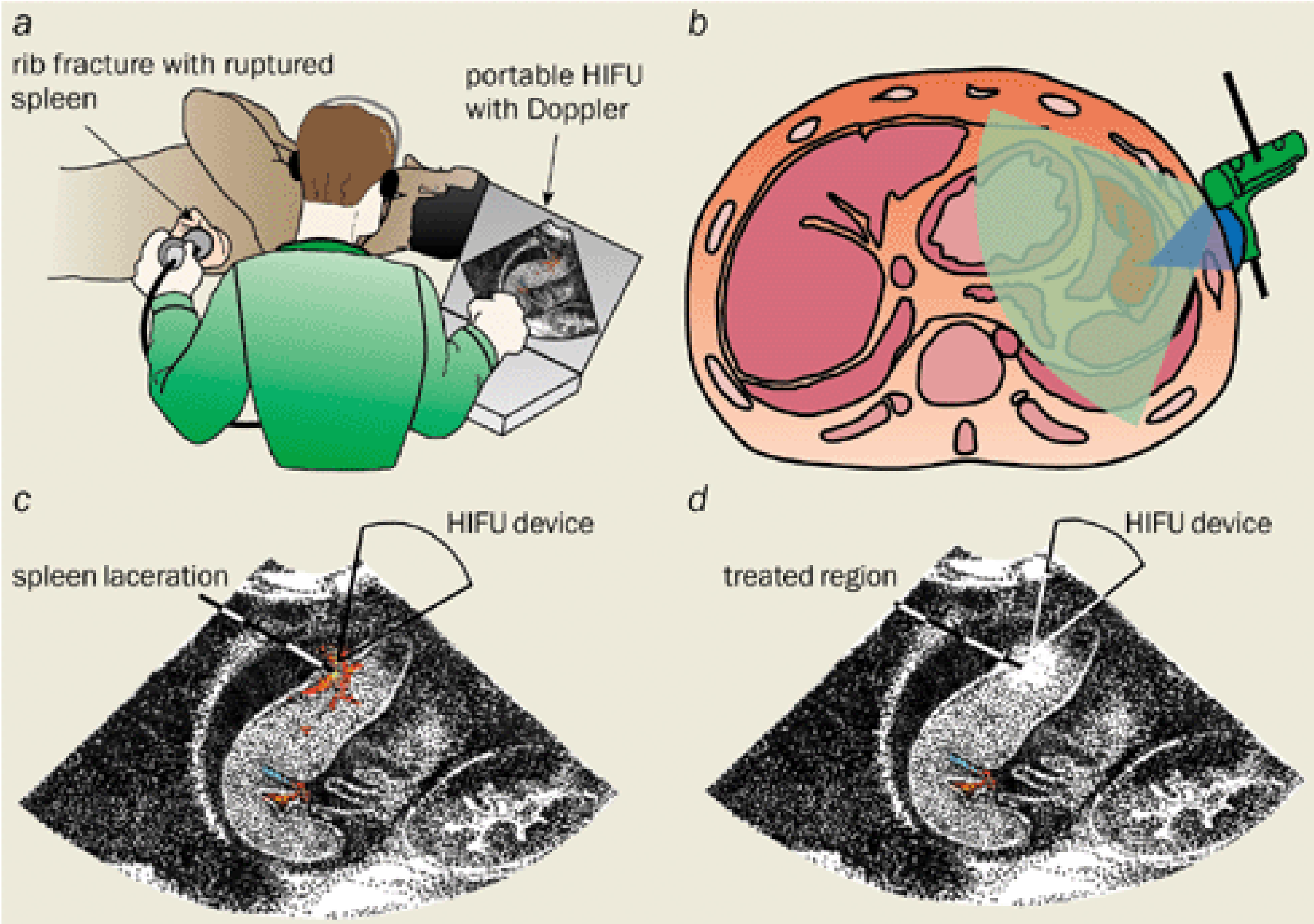
Prostate thermal therapy with interstitial and transurethral ultrasound applicators

Focused Ultrasound hemostasis and vascular occlusion



Invasive surgery could be avoided by using high-intensity focused ultrasound to treat internal bleeding.

超声治疗



How image-guided ultrasound could treat a casualty with an injured spleen.

(a) The injured patient is scanned using ultrasound imaging.

(b) The anatomical cross-sectional of the injured spleen. The ultrasound-imaging probe (green) and high-intensity ultrasound device (blue) are coupled together to guide the focal point of the acoustic energy during treatment.

(c) An ultrasound image of the spleen before treatment shows lacerations and bleeding.

(d) After treatment the bleeding has stopped. The bright region on the diagnostic ultrasound image of the spleen indicates the treated region.

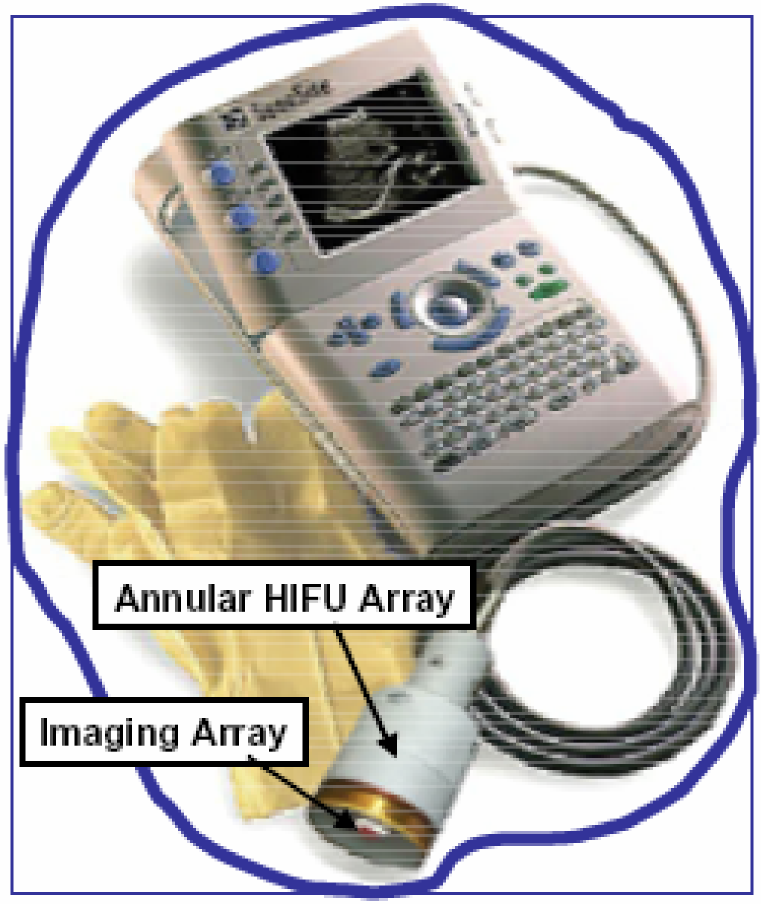
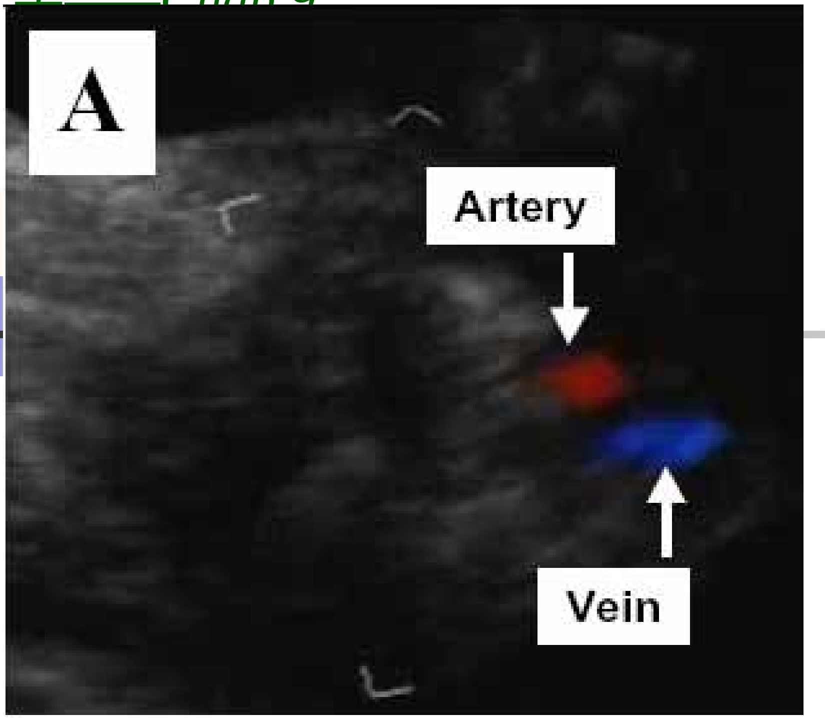
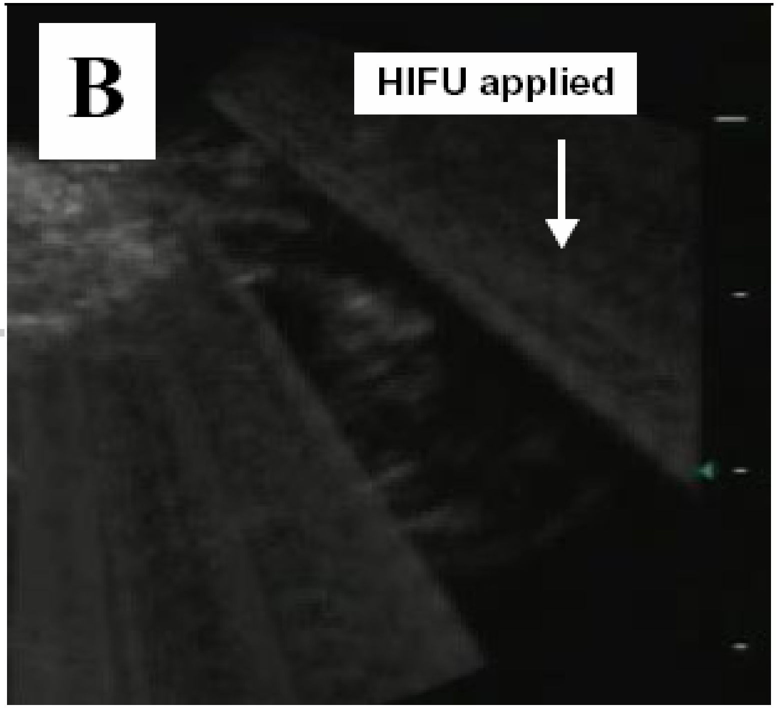
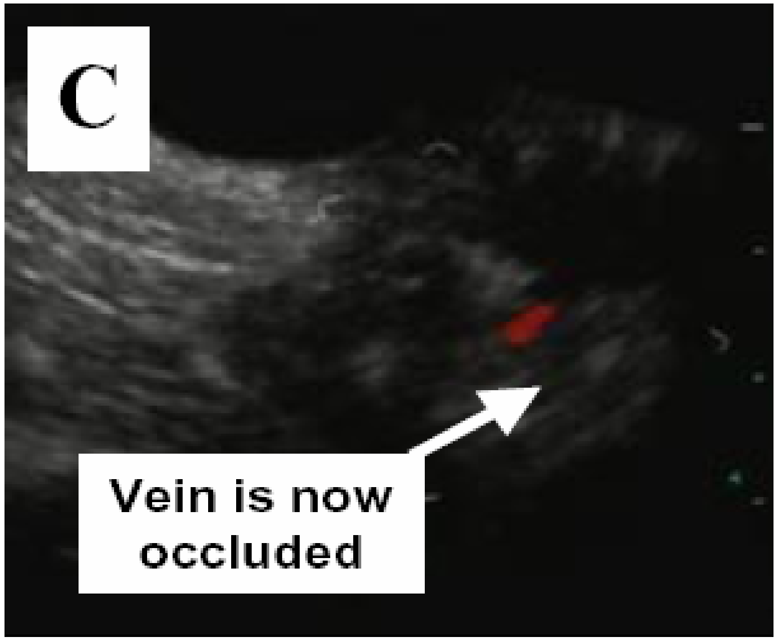


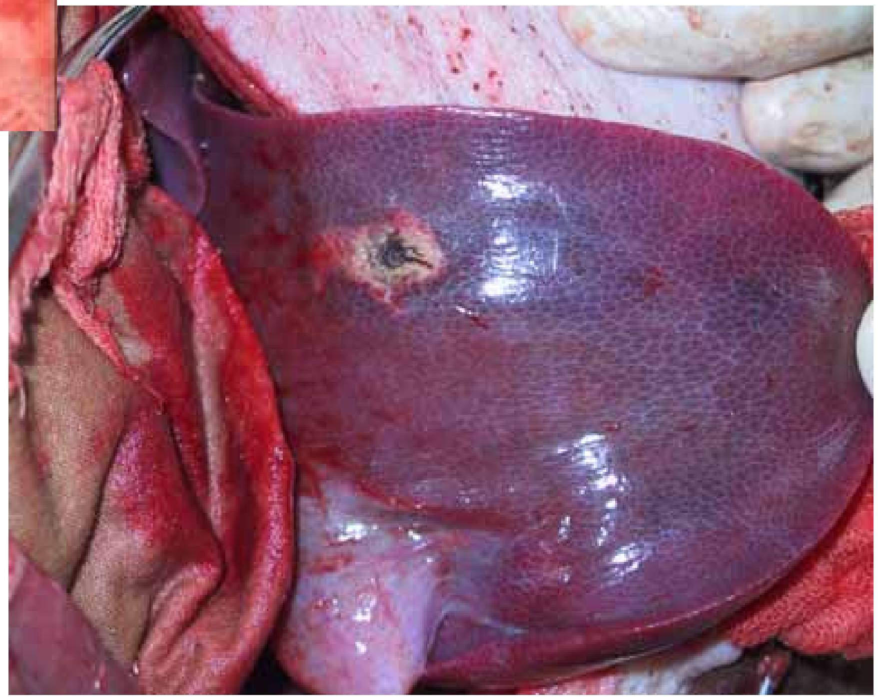
Fig. 8. Potential configuration of an image-guided, transcutaneous acoustic hemostasis system.



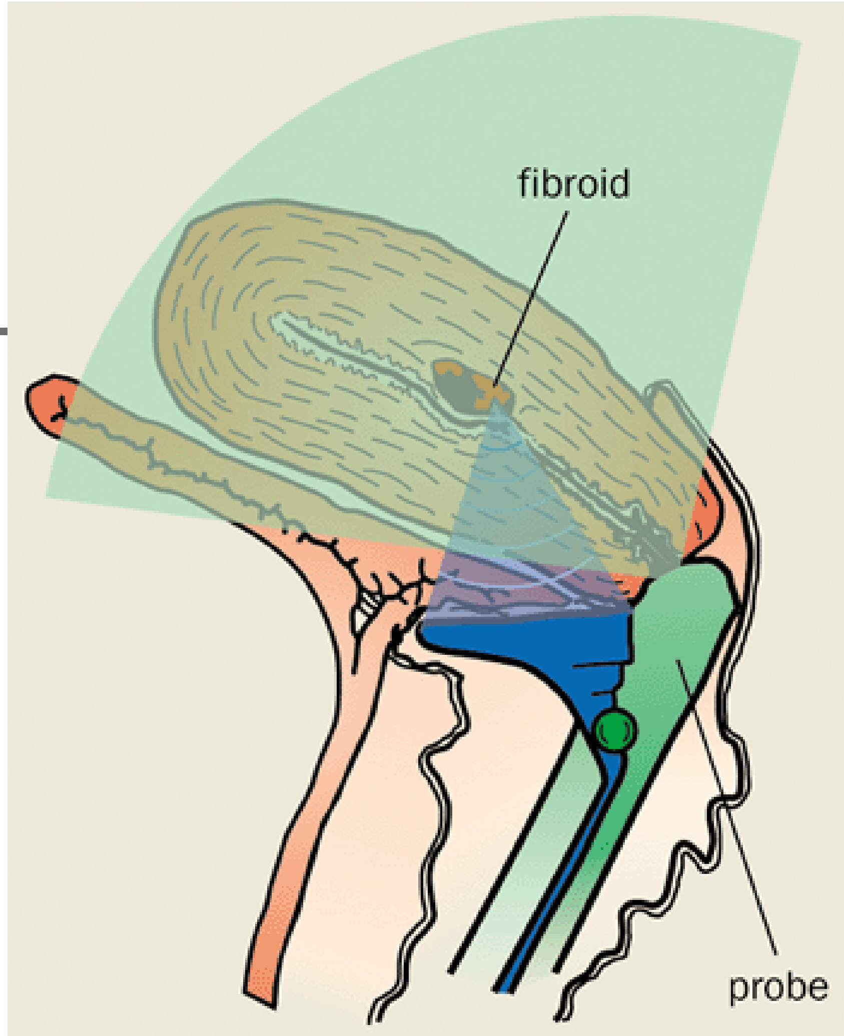




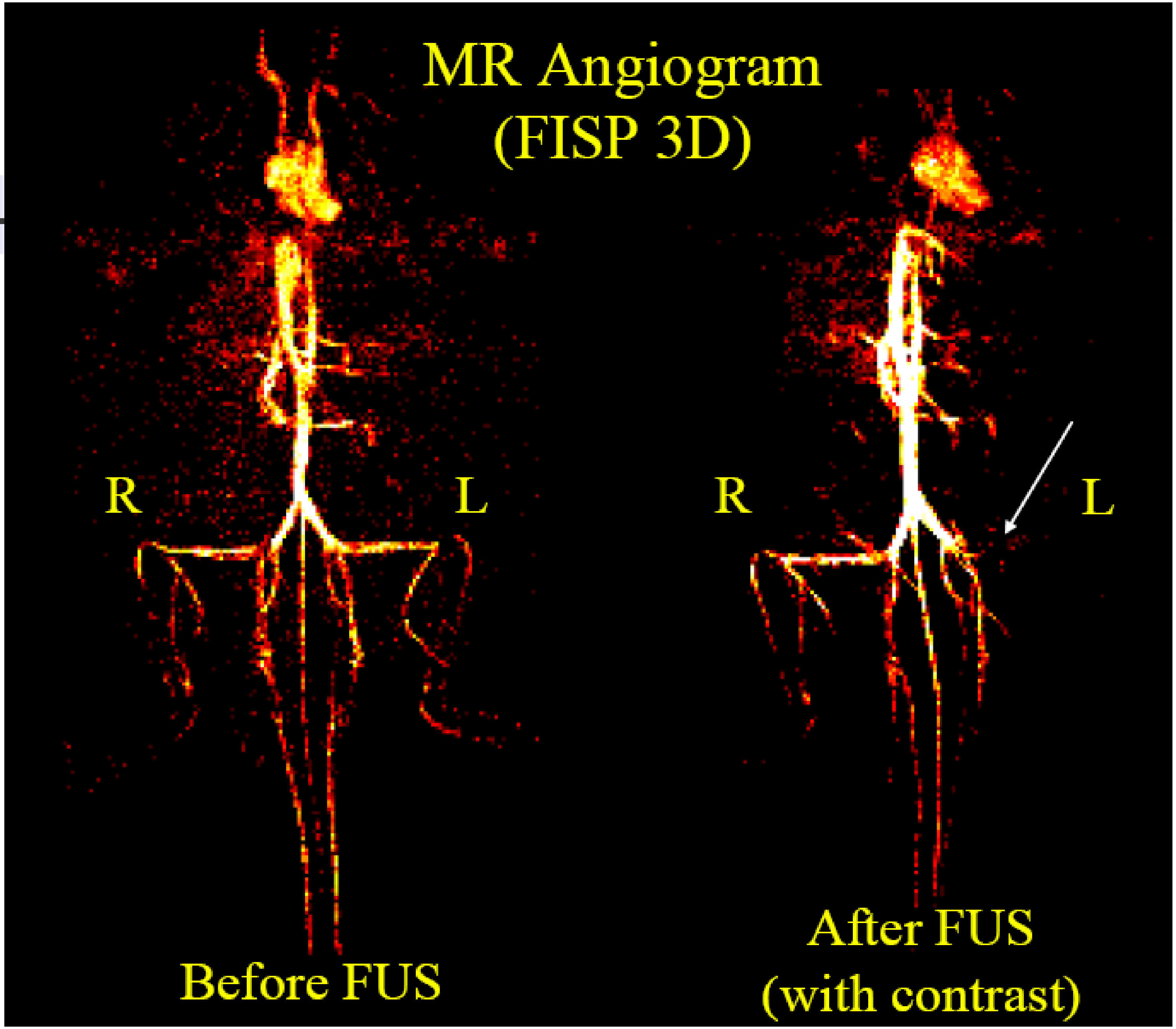
Demonstration of successful application of image-guided HIFU for vessel occlusion, using a device similar to that shown in Fig. 5. In A, the Doppler imaging system is used to identify a vein that is supplying a region of hemorrhage in a porcine liver; in B, the vessel is targeted and HIFU is applied; in C, rescanning with Doppler, the vein in question shows no flow and thus by implication is occluded. In this manner, rather than treating the entire region of hemorrhage, the vessels supplying the region of bleeding are effectively embolized.



- ✓Trauma
- ✓fetal medicine
- ✓Postpartum hemorrhage



The transvaginal imaging probe provides a real-time image of the uterus and the fibroids. Meanwhile, a burst of high-intensity focused ultrasound waves (blue) closes the vessels that supply the blood to the tumours and thereby destroys them.


MR Angiogram
(FISP 3D)
R
L
R
L
Before FUS
After FUS
(with contrast)

Laparoscopic High Intensity Focused Ultrasound: Application to Kidney Ablation

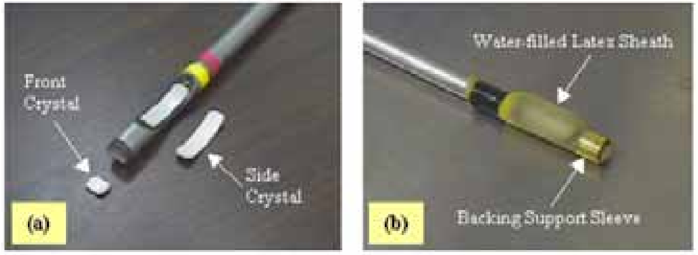


FIGURE 1. (a) The hand-held laparoscopic HIFU probe and the piezoceramic crystals shown separately. (b) A close-up of the probe tip covered by the coupling latex sheath.

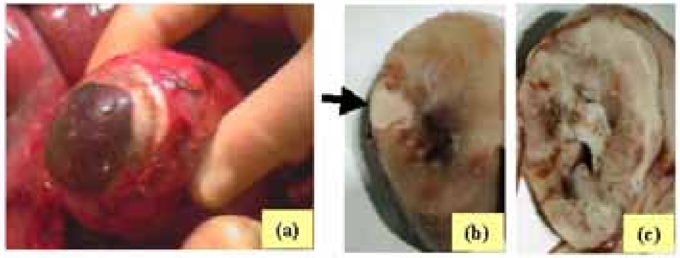


FIGURE 6. (a) 3-day post treatment view of the circumferential HIFU lesion created in the kidney's lower pole. (b) Cut section of the kidney through a single lesion. The arrow shows direction of the HIFU beam. (c) Cut section of the kidney through a complete circumferential lesion to show the uniformity of the lesion extending from the pelvic system to the capsule.

FIGURE 4. (a) The computer-controlled laparoscopic HIFU probe and the supporting sleeve, (b) a close-up of the probe tip covered with the supporting sleeve and the water-filled latex sheath, (c) Sonablate® 200 HIFU device, and (d) Sonablate® 500 HIFU device.

Ultrasound Imaging–Guided Noninvasive Ultrasound Thrombolysis

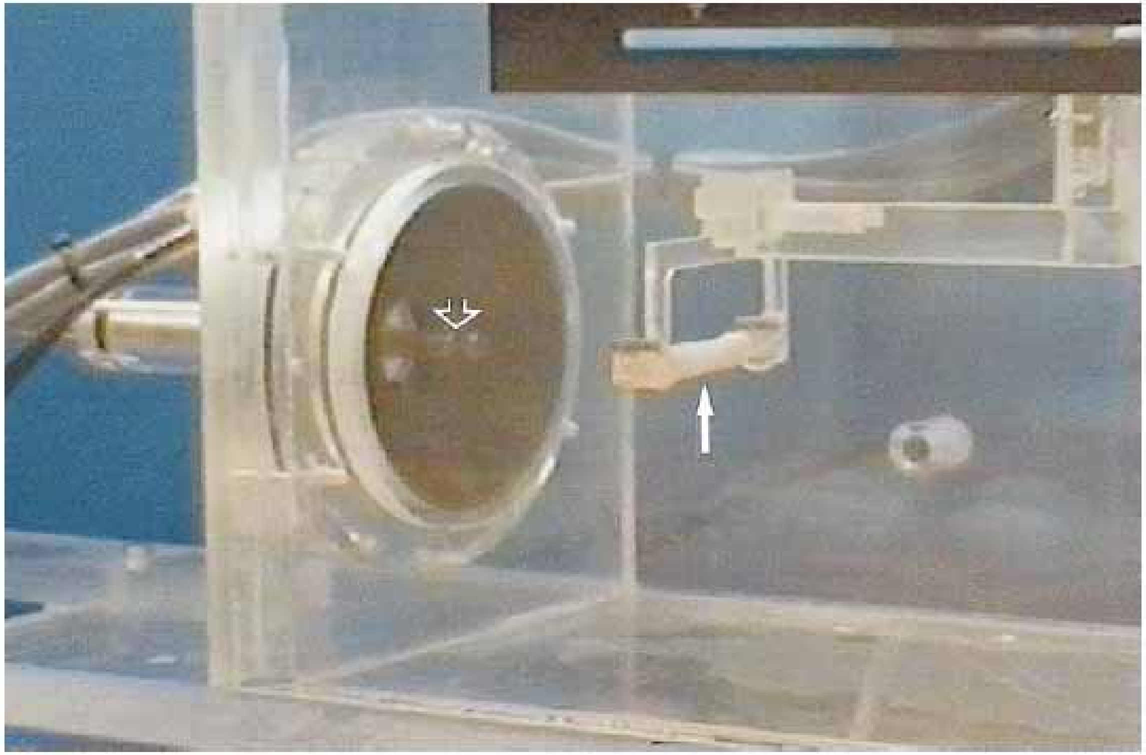


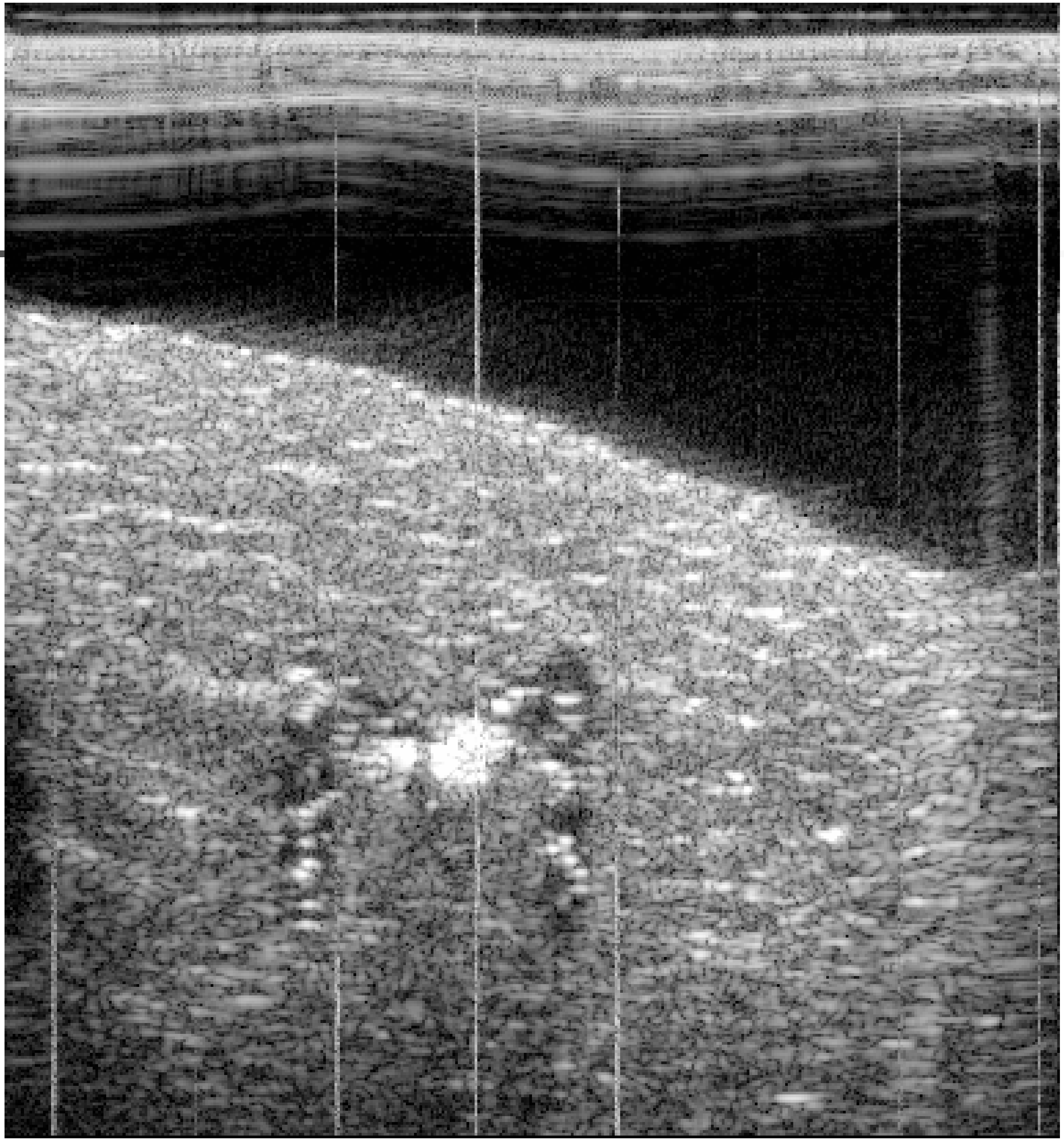
Figure 1. In vitro experimental setup. Bovine carotid artery segments (arrow) with intraluminal clots were mounted on U-shaped frame and immersed in tank filled with degassed, deionized water. One end of clot-artery preparations was positioned at focal area of acoustic lens parallel to plane of transducer. During sonication, vessel was moved in plane parallel to transducer with X-Y computerized positioning system. Procedure was monitored by online ultrasound imaging element of therapeutic transducer (open arrowhead).

Background—Catheter-based therapeutic ultrasound thrombolysis was recently shown to be effective and safe. The purpose of this work was to study the safety and efficacy of external high-intensity focused ultrasound thrombolysis guided by ultrasound imaging in experimental settings.

HIFU Ablation of thyroid nodules

组织摧毁术（histotripsy）

高强聚焦超声（HIFU）的治疗机理主要是利用瞬时高温效应。最近Cain提出，利用脉冲HIFU空化的机械作用，可以如同体外碎石术（lithotripsy）一般，将人体内的病变（如肿瘤）组织一点一点逐渐累积式地加以摧毁。这种想法是基于，通过对微泡以及脉冲高声强和时间平均低声强的HIFU多种参数的调节，足可以做到对空化阈值和空化事件的发生得到控制和调整。Cain还指出，由于空化的可控和可视（监测），它可能会使在许多治疗领域发挥作用，形成所谓的“空化治疗”的全新领域。



声孔效应 -- sonoporation

1997年**Bao**等人的研究表明，使用低声压（**0.2MPa**）超声波对中华大田鼠卵巢细胞（**Chinese hamster ovary cells**）的含微泡悬浮液（**10% Albunex**，气泡/细胞=**40**）进行辐照时，细胞膜就可以对大分子暂时开放，随后再闭起来。在细胞膜暂时开放的时间里，细胞外面的大分子就可以进入细胞，被细胞捕获，并称此现象为声孔效应*(细胞膜的通透性)*

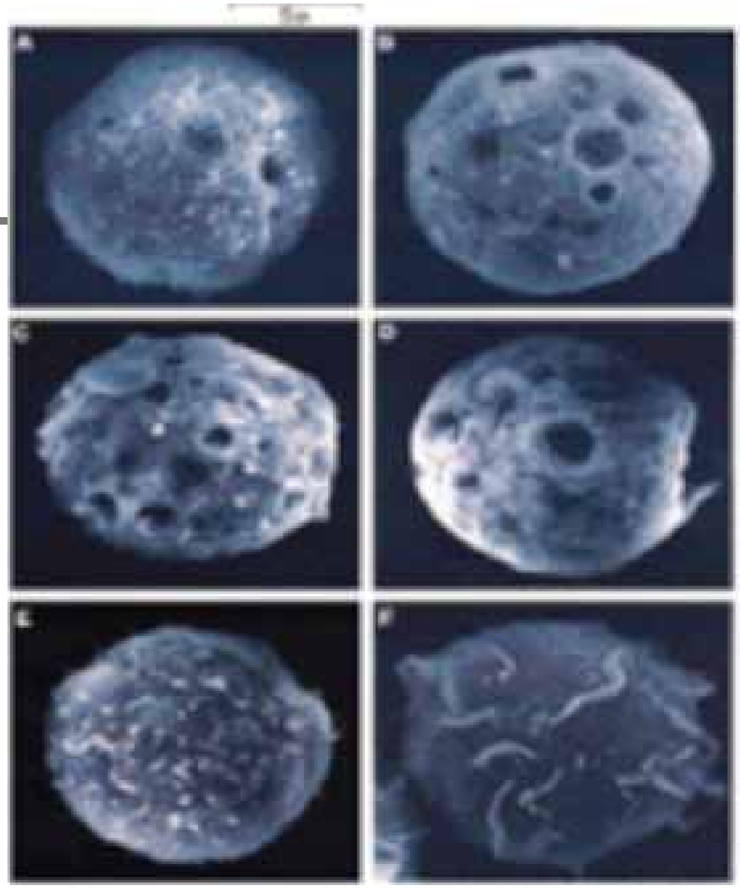
1998年 **Greenleaf** 指出，声孔效应可能在基因疗法中成为基因注入的新型的技术基础.

进一步研究表明，声孔效应主要是通过声空化机制来实现的。这预示： 造影剂则可能在基因治疗领域中发挥巨大作用.！

2000年 Junru Wu（吴君如）等人报道，使用淋巴细胞悬浮液，引入造影剂（option)且使其浓度可变，他们在实验中观察到了两种声孔效应，即可修复性声孔效应和致死声孔效应. 且认为，这两种效应来自同一种机制，是同一种机制作用程度不同的两种表现形式。

Wu的实验表明：在相同的声辐照条件下，造影剂浓度低，即气泡距细胞距离大，表现为可修复性声孔效应；当辐照时间延长，或造影剂浓度增大使气泡与细胞间距减少，使细胞膜上发生的声孔无法修复时，即转向致死性声孔效应。文中详细研究了这两种声孔效应与细胞浓度、气泡数量及声辐照参数之间的关系.

声空化效应为什么会导致声孔效应呢？这是因为微气泡在声波作用下表现出稳态空化伴随发生的微声流作用，使其周围的组织细胞壁和质膜被击穿，产生可逆或非可逆的小孔.



Scanning electron microscopic images of HL-60 cells
Irradiated with ultrasound in the presence of MC 540 (A to D), untreated intact cells (E), cells irradiated with ultrasound alone (F).

Tachibana et al. Lancet 353:1409 (1999)

Sonophoresis

术语解释：

* **Sonophoresis** --- 声电泳 （如同 Sonochemistry译为声化学）

* **Phoresis** ---- 电泳

* 电泳：在分散体系中，带电的分子或颗粒（如蛋白、核酸等）在外加电场作用下向电极移动的现象。

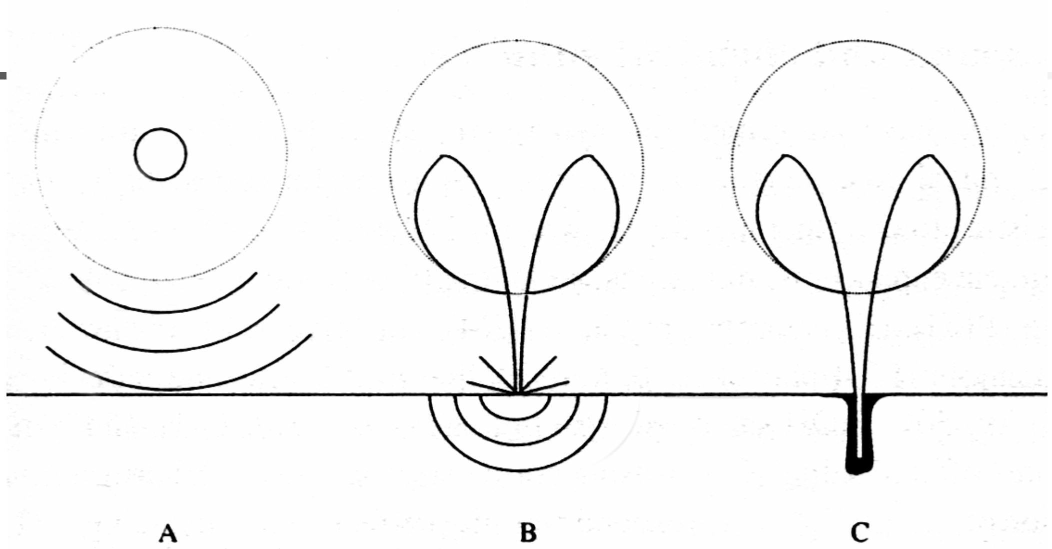
经皮施药是一种具有吸引力的施药方式，但它却因为皮肤通透性小而使应用受到限制，为了解决这个问题，发现“超声波作用可以增强皮肤的通透性”，即所谓的“声电泳”。进而发现小于**100kHz**的低频超声更为有效。

低频声电泳的作用机制

有关低频声电泳作用机制的探讨，倍受关注。

目前一致的看法是：在超声换能器与皮肤之间的超声耦合剂中的声空化—在声波作用下空化泡崩溃—是引起声电泳效应的原因。空化泡的最大半径与超声波频率和声压大小有关，对于 频率为20-100kHz,声压为1-2.4 bar，最大半径为10-100μm.

通常，空化分为稳态和瞬态空化2种，它们与声电泳的关系见下图 。



如图所示，有3种可能瞬态空化模式影响皮肤通透性：

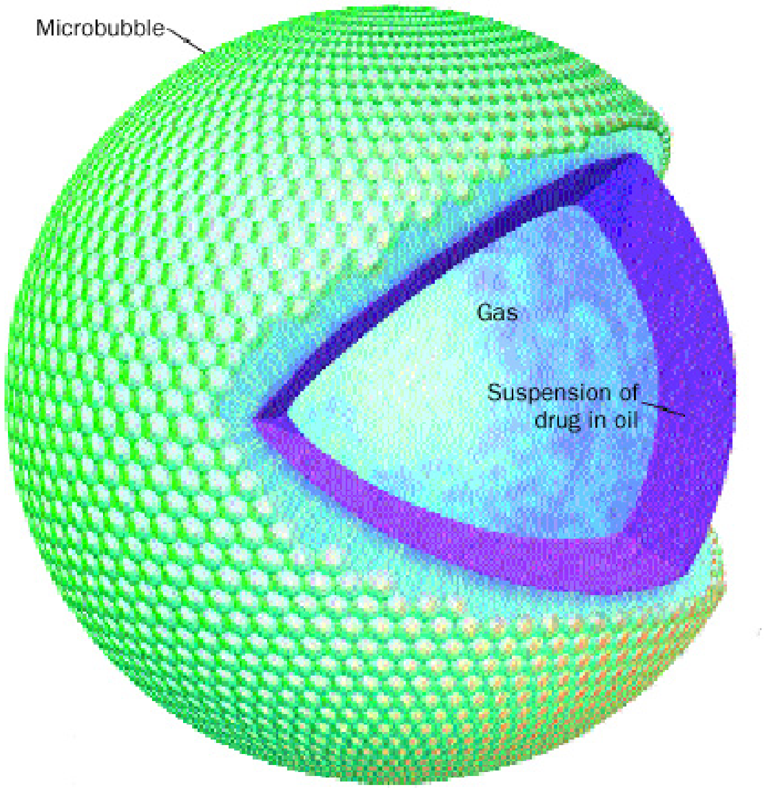
A　皮肤附近的圆形空化泡崩溃产生的冲击波,它可以破坏皮肤的双脂层；

B　声冲流对皮肤表面的冲击，声冲流的半径约为空化泡最大半径的10倍，它通过干扰皮肤双脂层来改善其通透性。

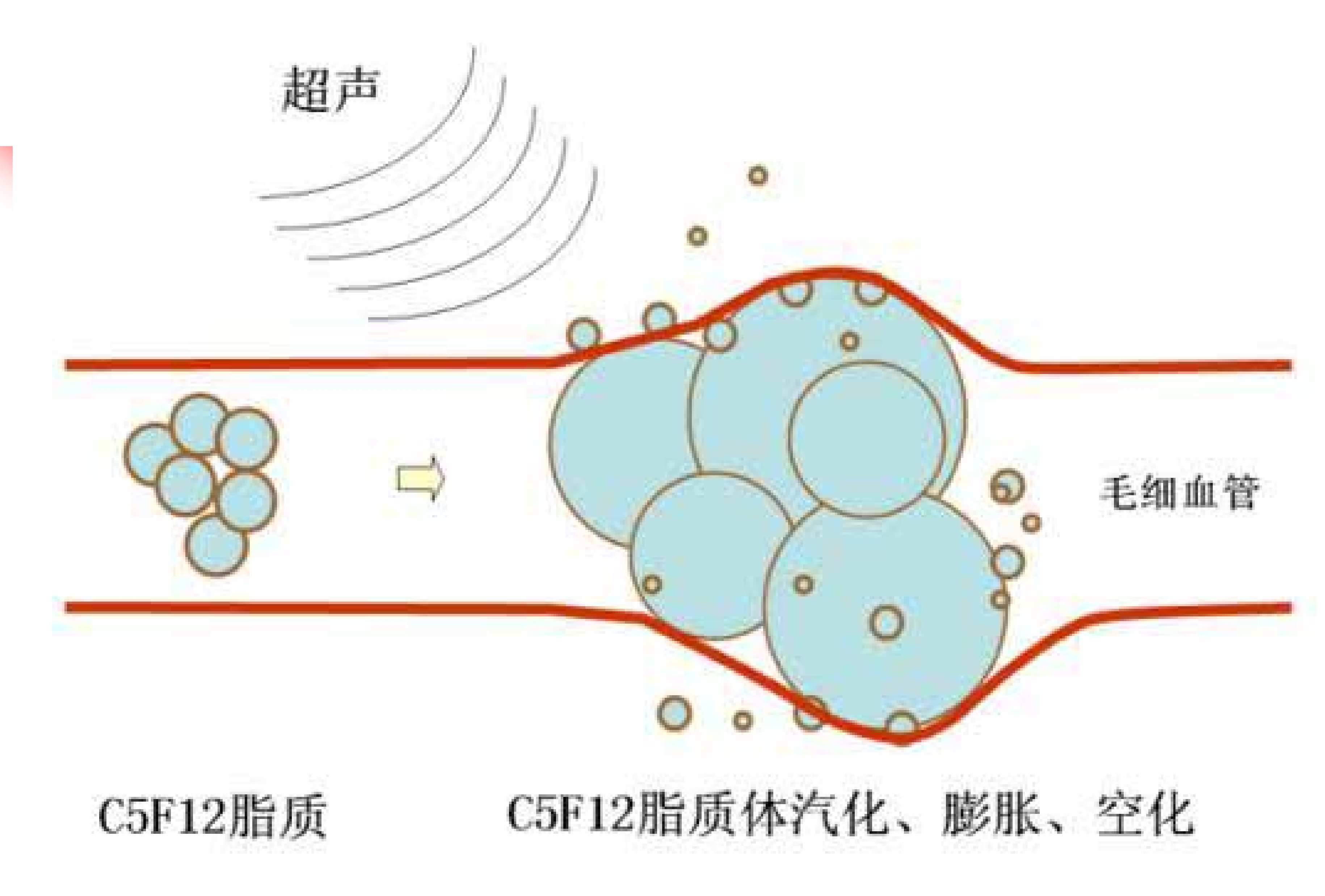
C　有时，声冲流也可能穿透皮肤，以增强其通透性。

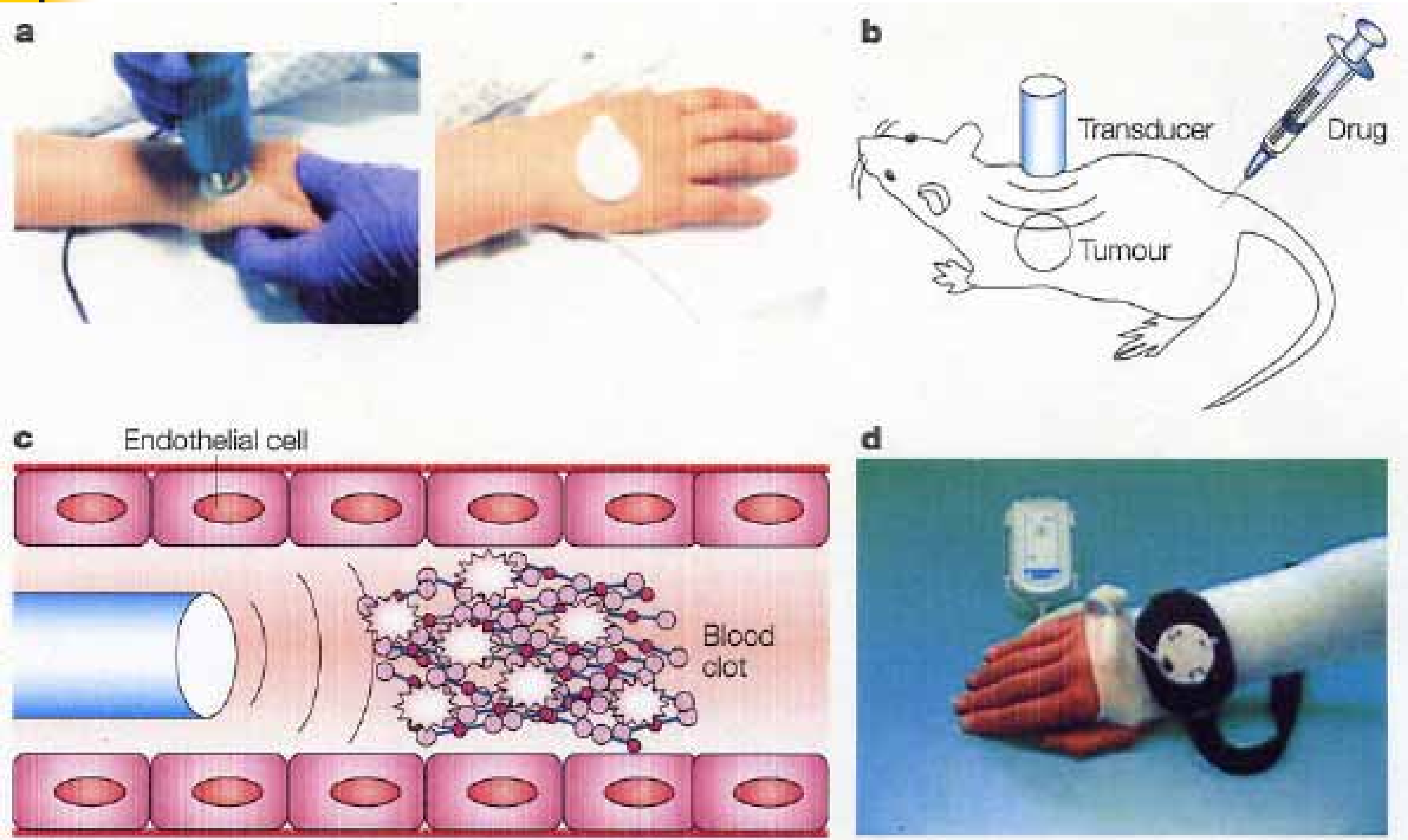
进一步研究表明，声电泳与其他增强机制（化学电泳、离子电泳）协同作用，会使药物穿透性更好。

Enhancing drug deliver and gene transfer

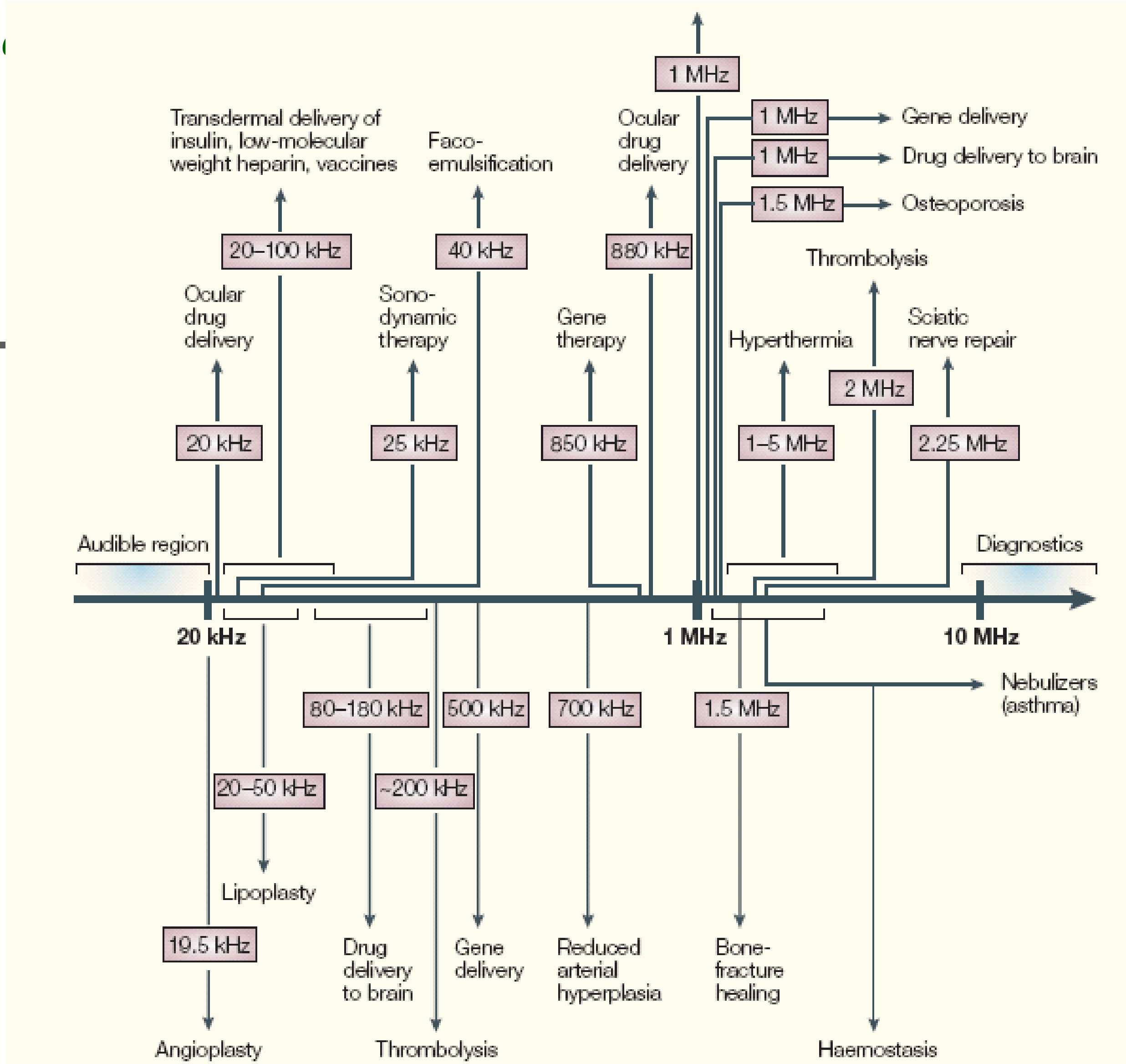


Drugs and other biocompatible materials may be incorporated into acoustically active carriers that can be ruptured by ultrasound, increasing the rate of energy transfer into adjacent tissue or fluids.


超声
毛细血管
C5F12脂质
C5F12脂质体汽化、膨胀、空化



Mitragotri S.. Nature Reviews Drug Discovery 4, Mar 2005



Samir Mitragotri . Innovation: Healing sound: the use of ultrasound in drug delivery and other therapeutic applications. Nature Reviews Drug Discovery 4, 255-260 (01 Mar 2005)

In Feb. 2004, the US congress gathered 30 top scientists of the world to discuss the frontier sciences, therapeutic ultrasound (HIFU technology) was discussed for the first time.


Silent sound zaps cancer: Ultrasound cuts side effects when used to remove tumours.

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American Association for the Advancement of Science, Seattle, February, 2004

Silent sound zaps cancer

Ultrasound cuts side effects when used to remove tumours.

16 February 2004

JIM GILES

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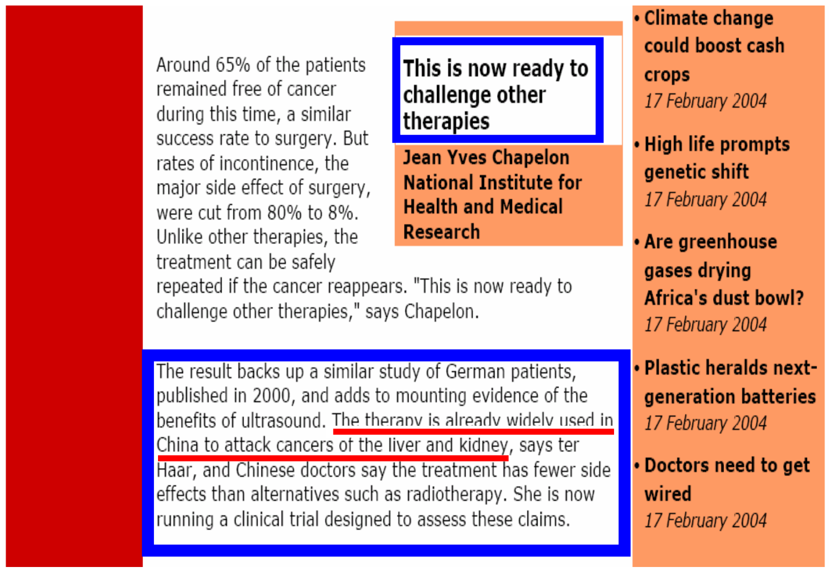
Around 65% of the patients remained free of cancer during this time, a similar success rate to surgery. But rates of incontinence, the major side effect of surgery, were cut from 80% to 8%. Unlike other therapies, the treatment can be safely repeated if the cancer reappears. "This is now ready to challenge other therapies," says Chapelon.

This is now ready to challenge other therapies

Jean Yves Chapelon National Institute for Health and Medical Research

The result backs up a similar study of German patients, published in 2000, and adds to mounting evidence of the benefits of ultrasound. The therapy is already widely used in China to attack cancers of the liver and kidney, says ter Haar, and Chinese doctors say the treatment has fewer side effects than alternatives such as radiotherapy. She is now running a clinical trial designed to assess these claims.

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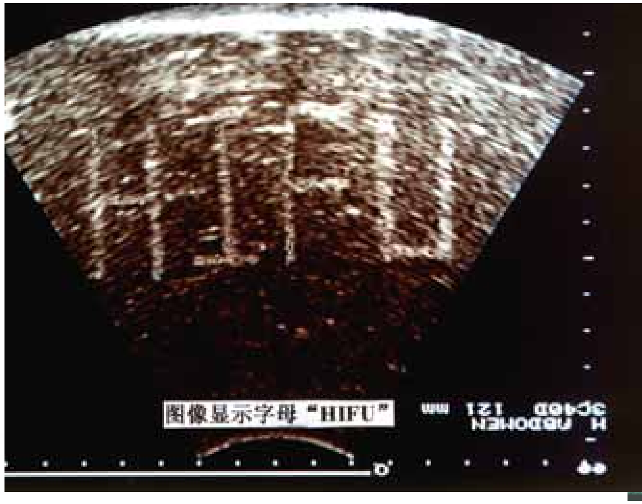
Giles J. Nature 2004, February 18

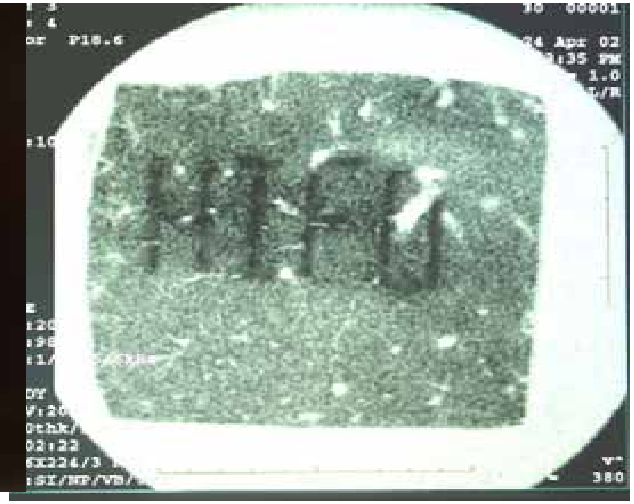
Perspective

HIFU's future depends on not only HIFU technology, but also a close collaboration between scientists, engineers and clinical doctors.

Coagulative necrosis of "HIFU" in ox liver



Ultrasound-imaging of "HIFU"



MRI –imaging of "HIFU"