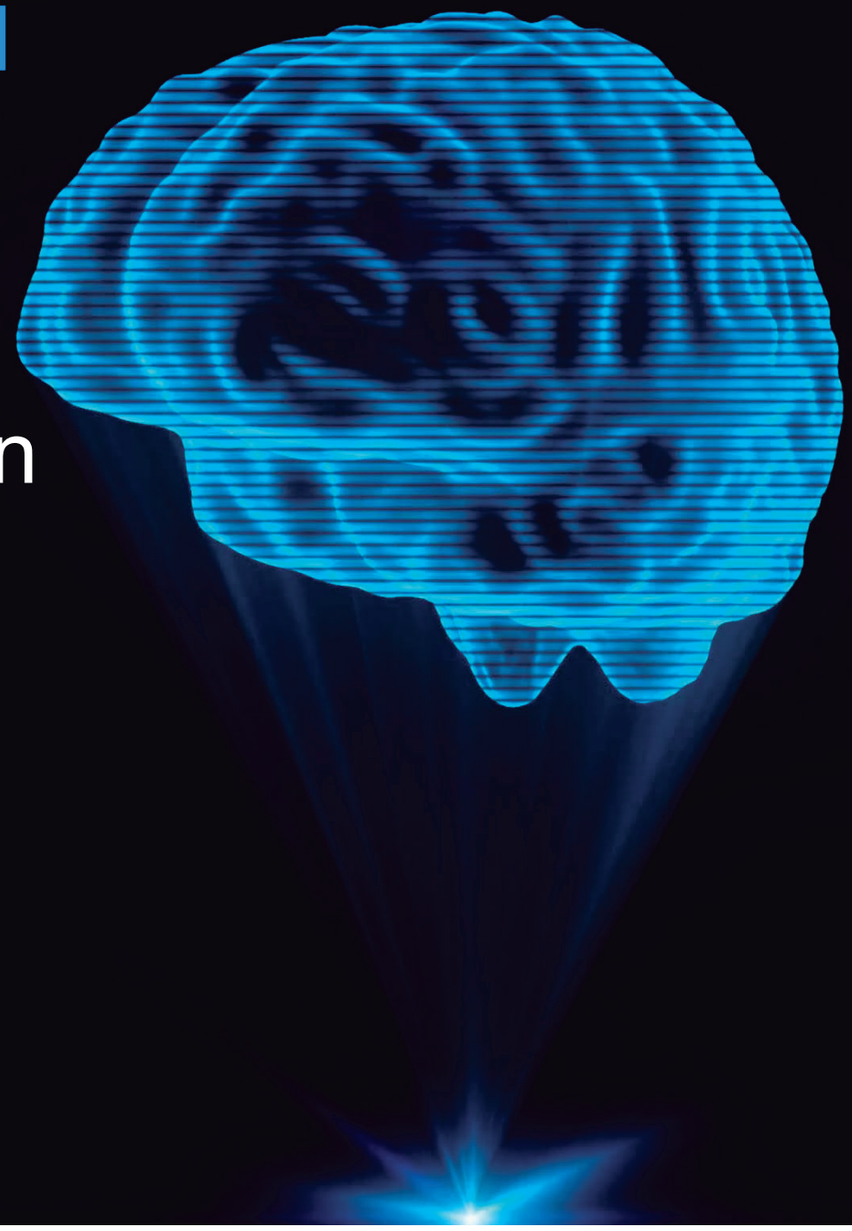
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Ultrasonic holograms in the brain

MEDAMI 2019. Valencia, 15-17 de mayo de 2019.

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Noé Jiménez
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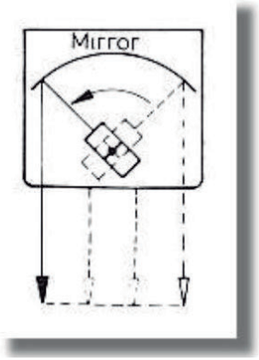
Contents

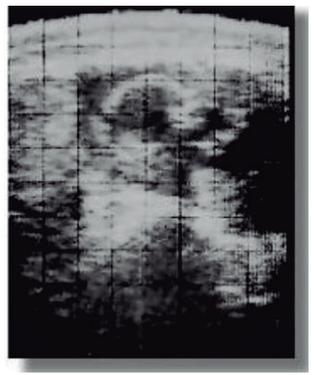
- **Ultrasound capabilities in biomedical.**
  - Neurological disease
- **How can we produce Focused Ultrasound?**
- **How do we introduce them in the brain?**
  - Skull distortion
- **Transcranial Ultrasound today**
  - Clinical and trials
- **One step forward: holograms for the brain**
- **Results**
- **Conclusions**

Ultrasound capabilities in biomedical

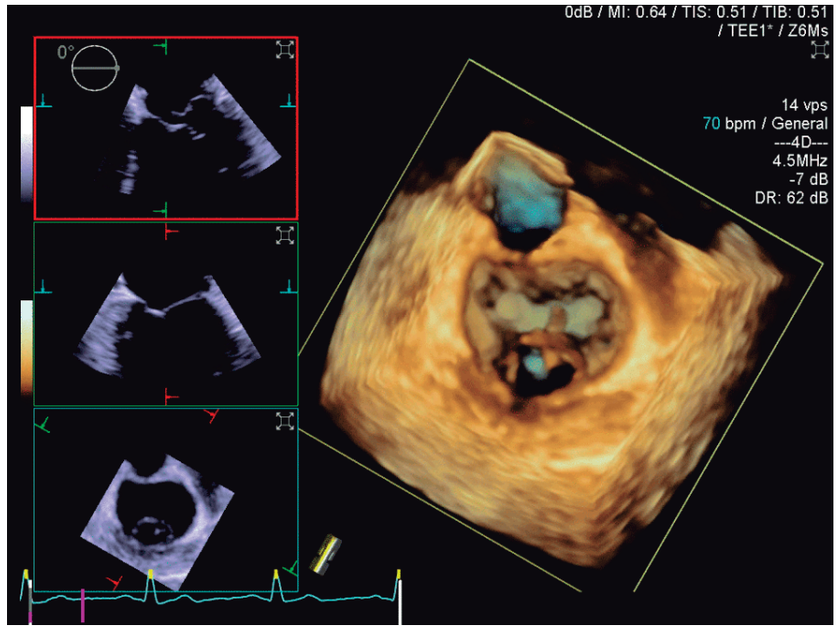
- Ultrasound Imaging is an essential **image** modality



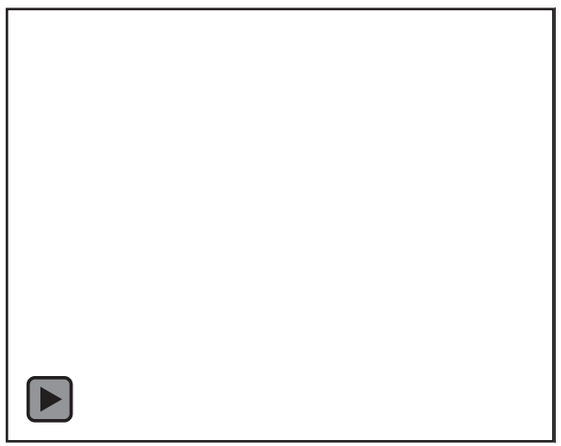




Vidoson, Siemens, 1967.

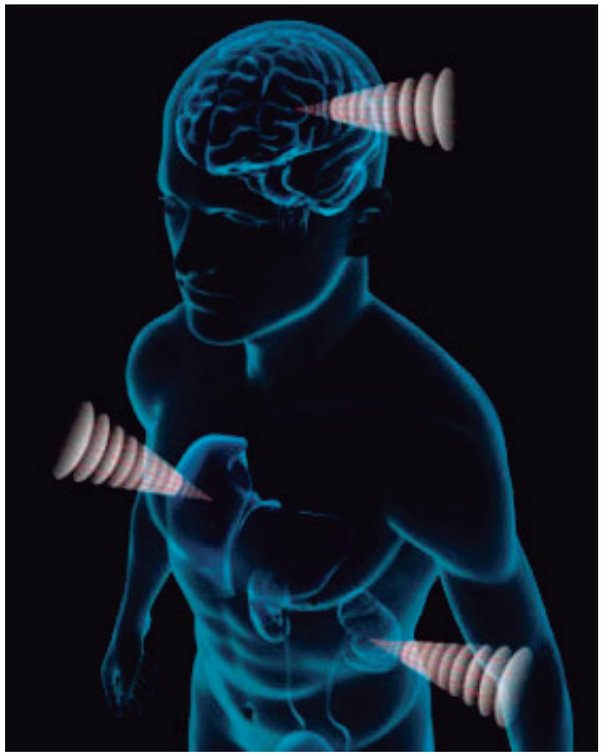






Ultrasound capabilities in biomedical

- Focused ultrasound is an early-stage, non-invasive **therapeutic** technology that could transform the treatment of many medical disorders



"The brain is the vanguard target for focused ultrasound"

Focused Ultrasound Fundation.

Anorexia
Fetal anomalies
Insulinoma
Colorectal tumors
Liver fibrosis
Local anesthesia
Trigeminal neuralgia
Multiple sclerosis
Stroke
...

Early Stage

Focused ultrasound research is in the laboratory phase and is not yet available for patients.

Clinical Trials

Focused ultrasound for this condition is being researched in clinical trials.

Alzheimer's Disease
Epilepsy
Amyotrophic lateral sclerosis
Glioblastoma
Holmes Tremor
Huntington's disease
Astrocytoma
Multiple tumors
...

Uterine Fibroids, 2004.
Bone metastasis, 2012.
Prostate cancer, 2015.
Temblor esencial, 2016.
Tremor-dominant Parkinson's disease, 2018.

FDA Approved

The US Food and Drug Administration has approved focused ultrasound for this condition. Patients can seek commercial treatment at participating sites.

International Approval

Focused ultrasound is approved to treat this condition outside the US. Patients can seek commercial treatment at participating international sites.

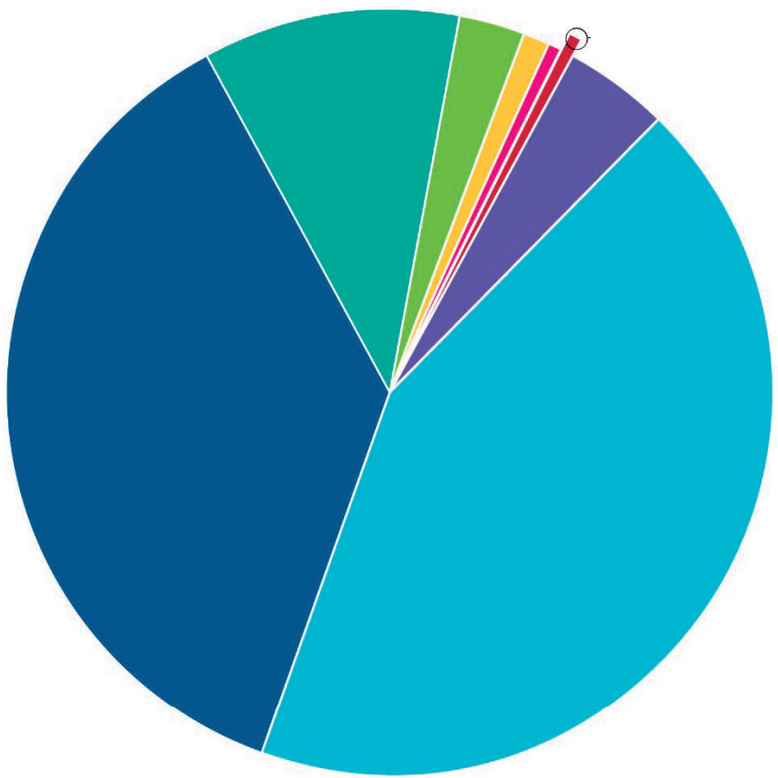
Depression
Neuropathic pain
Obsess-comp disorder
Parkinson's disease
Liver tumors
Pancreatic tumors
Soft tissue tumors
Breast cancer
...

Ultrasound capabilities in biomedical

Treated Patientes:

- Total: 167,993 (2018)

All Indications

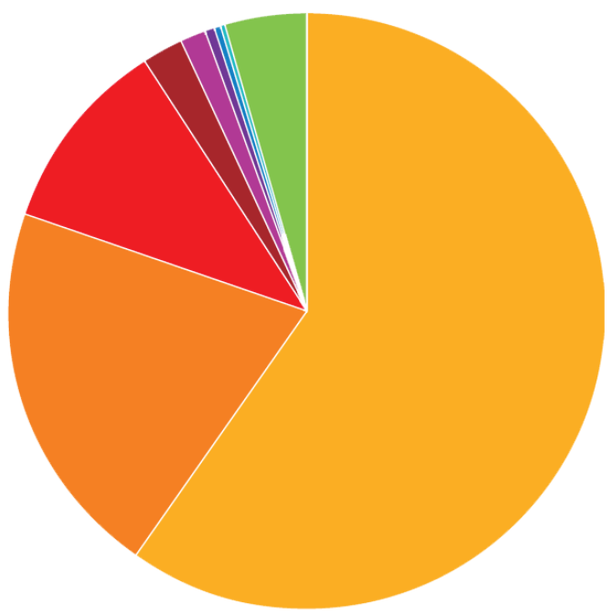


Uterine fibroids	72,488	43%
Prostate diseases	61,749	37%
Liver cancer	18,000	11%
Glaucoma	4,900	3%
Bone metastases	1,602	>1%
Breast cancer	1,269	>1%
Brain	868	>1%
Others*	7,117	4%

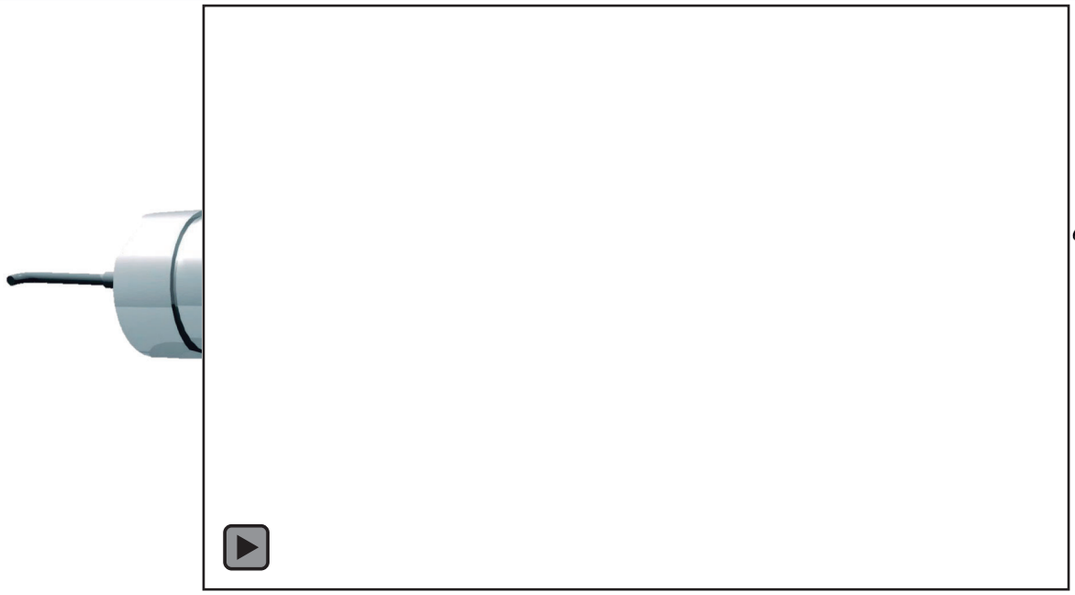
868 Total Brain Treatments

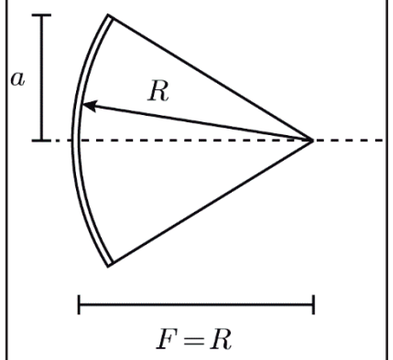
Essential Tremor	519	60%
Parkinson's disease	179	21%
Neuropathic pain	91	10%
Brain tumors	19	2%
Obsessive-compulsive disorder	14	2%
Depression	5	>1%
Dystonia	3	>1%
Epilepsy	1	>1%
Unspecified**	37	4%

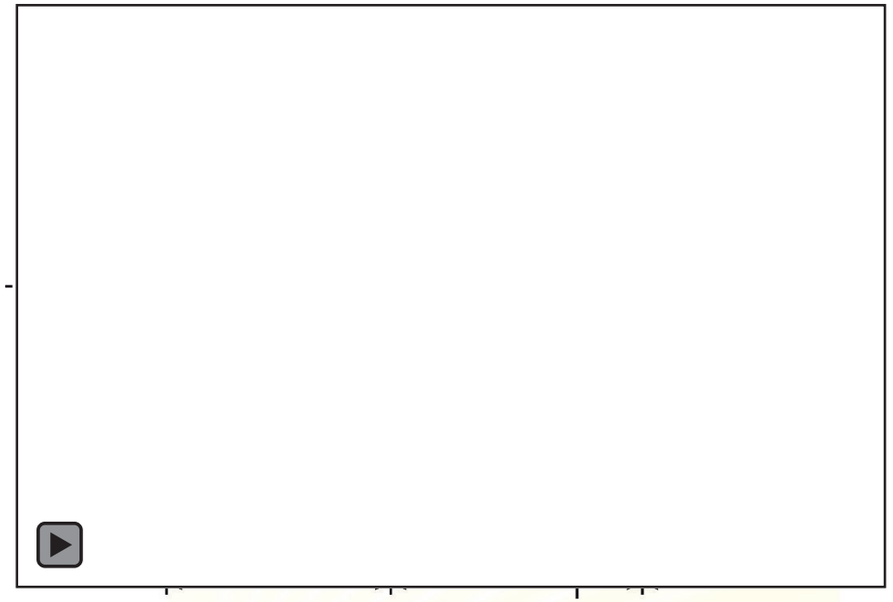
Brain Indications



How can we produce Focused Ultrasound?

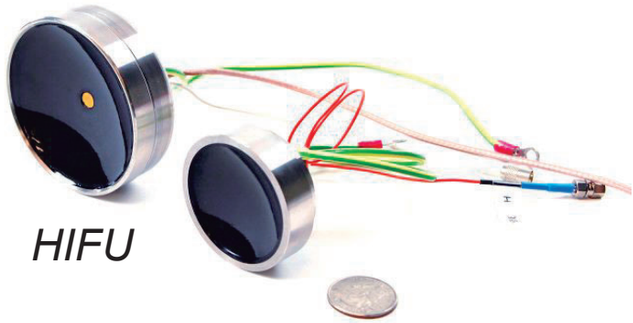


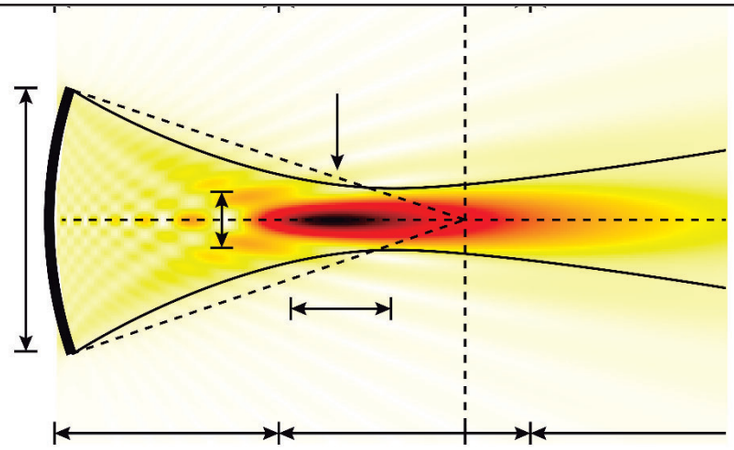




Single-element approach







How can we produce Focused Ultrasound?



Quite nice in water, but… Skull distortion!

Simulación con doble foco



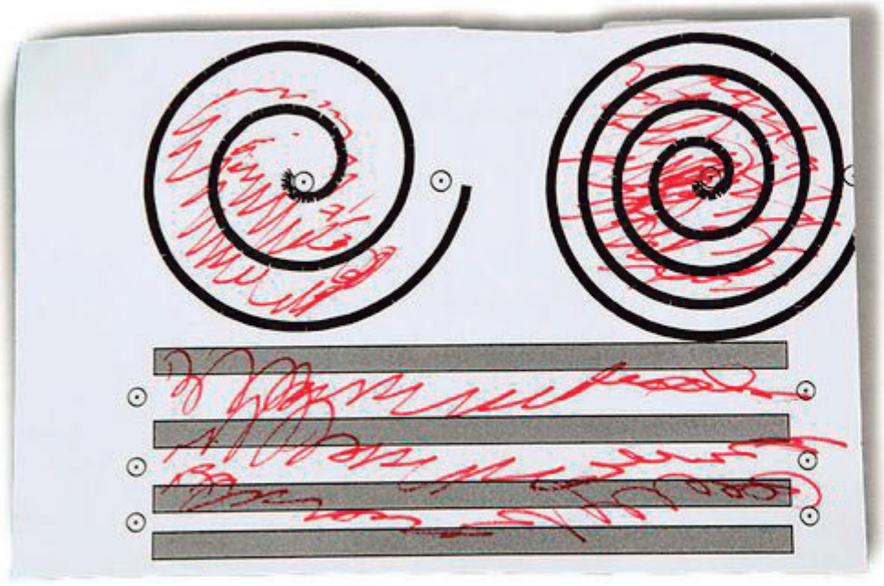
How can we produce Focused Ultrasound?

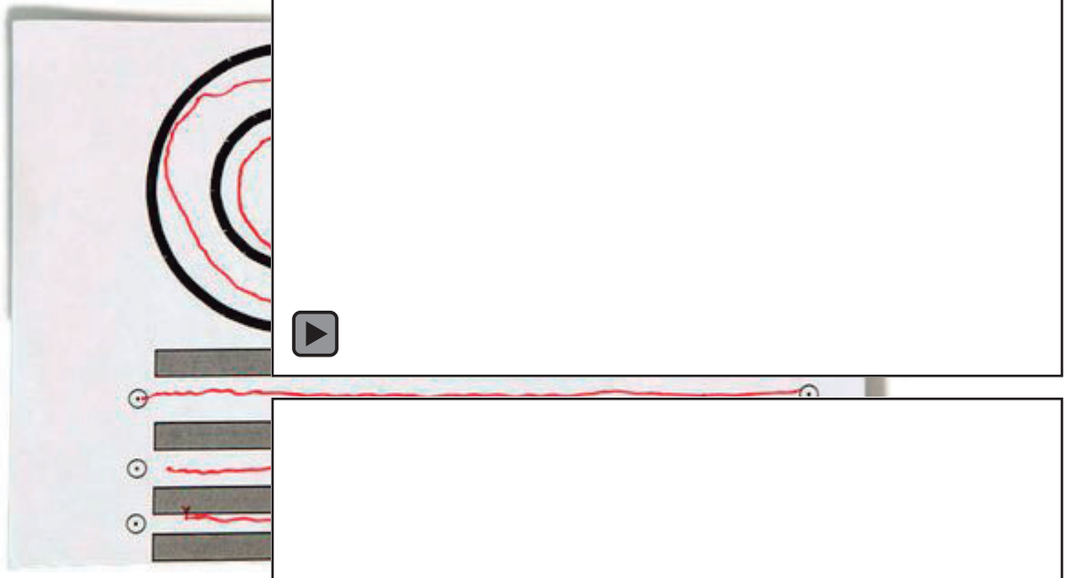
Transcranial Magnetic Resonance guided Focused Ultrasound (MRgFUS)

→ Thermal ablation of the thalamus

Pl

a



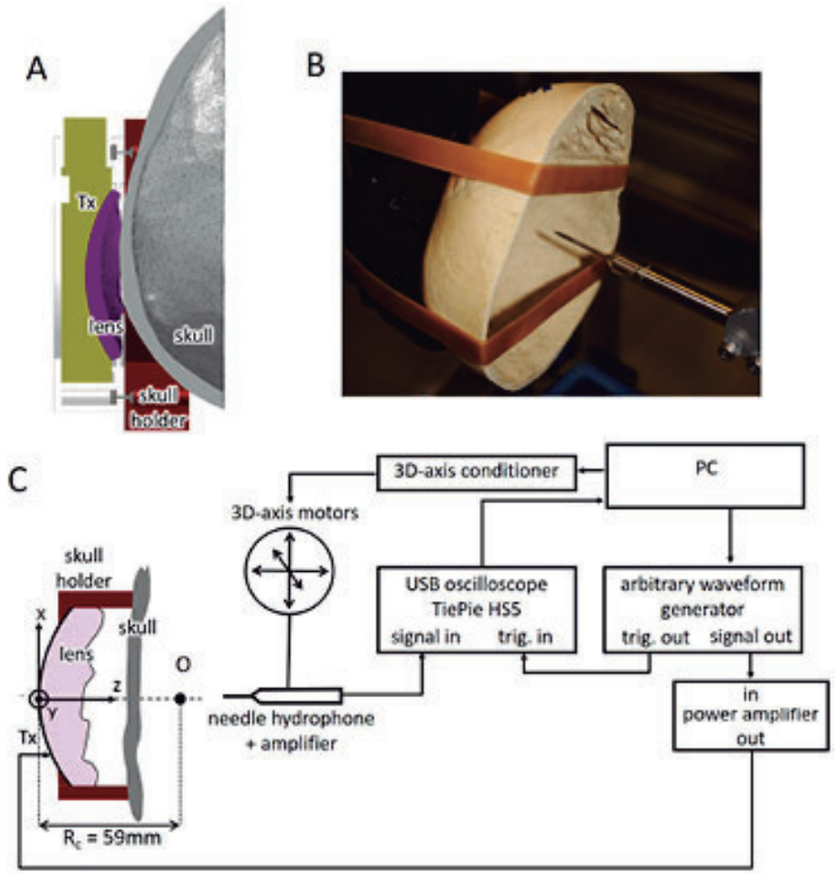


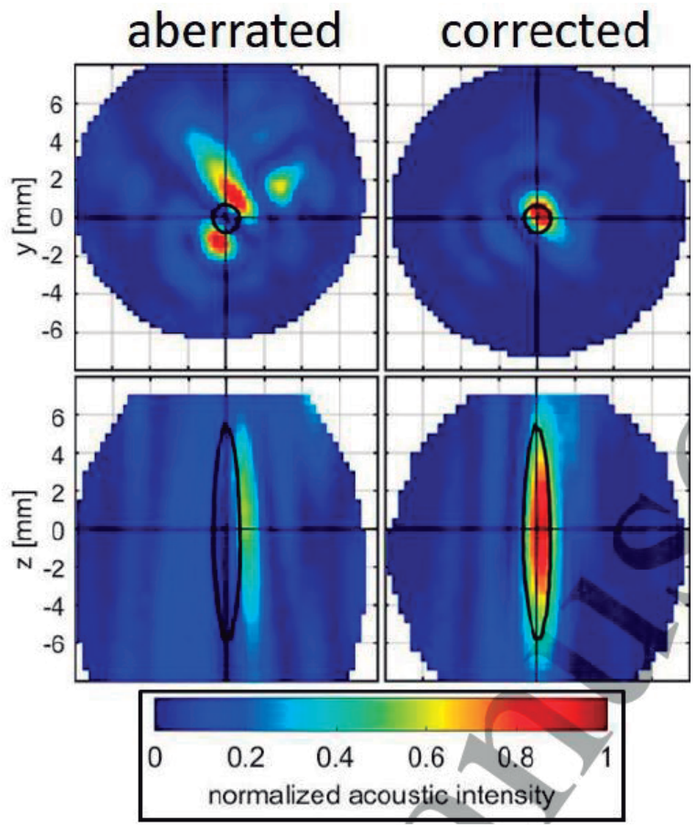




How can we produce Focused Ultrasound?

- Single-element + phase lens approach





Maimburg et al. Physics in Medicine & Biology 63(2) 2018.

Transcranial Ultrasound today

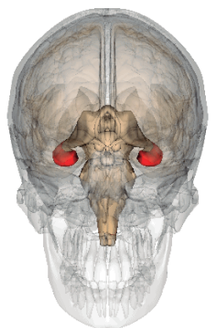
- All applications of transcranial ultrasound for neurological conditions, both clinical or trial, are limited to focusing on a single point with more or less accuracy.

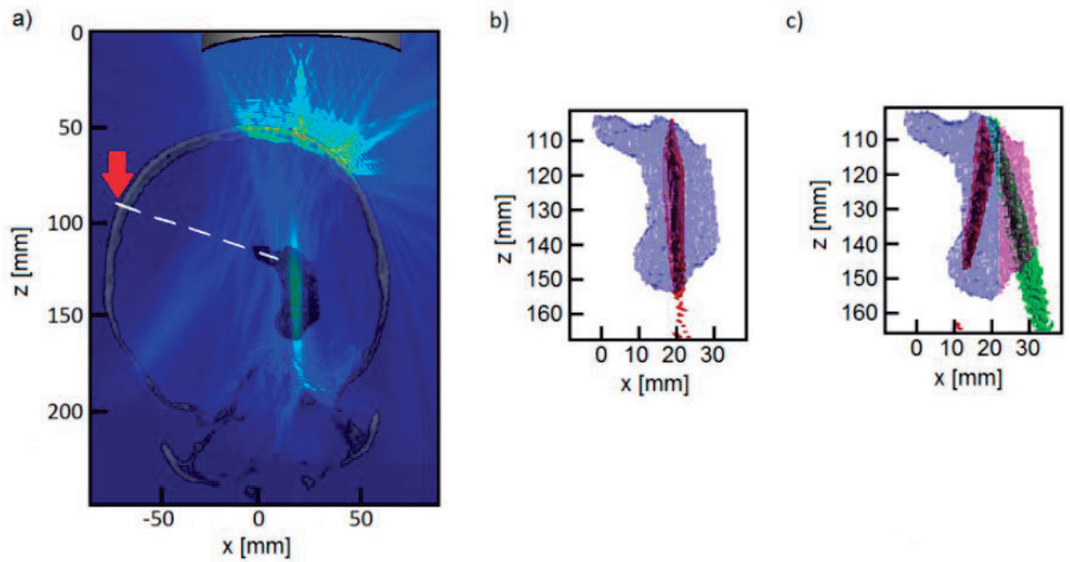
→

- But most of the neurological conditions affect complex structures in the brain: big volumes.

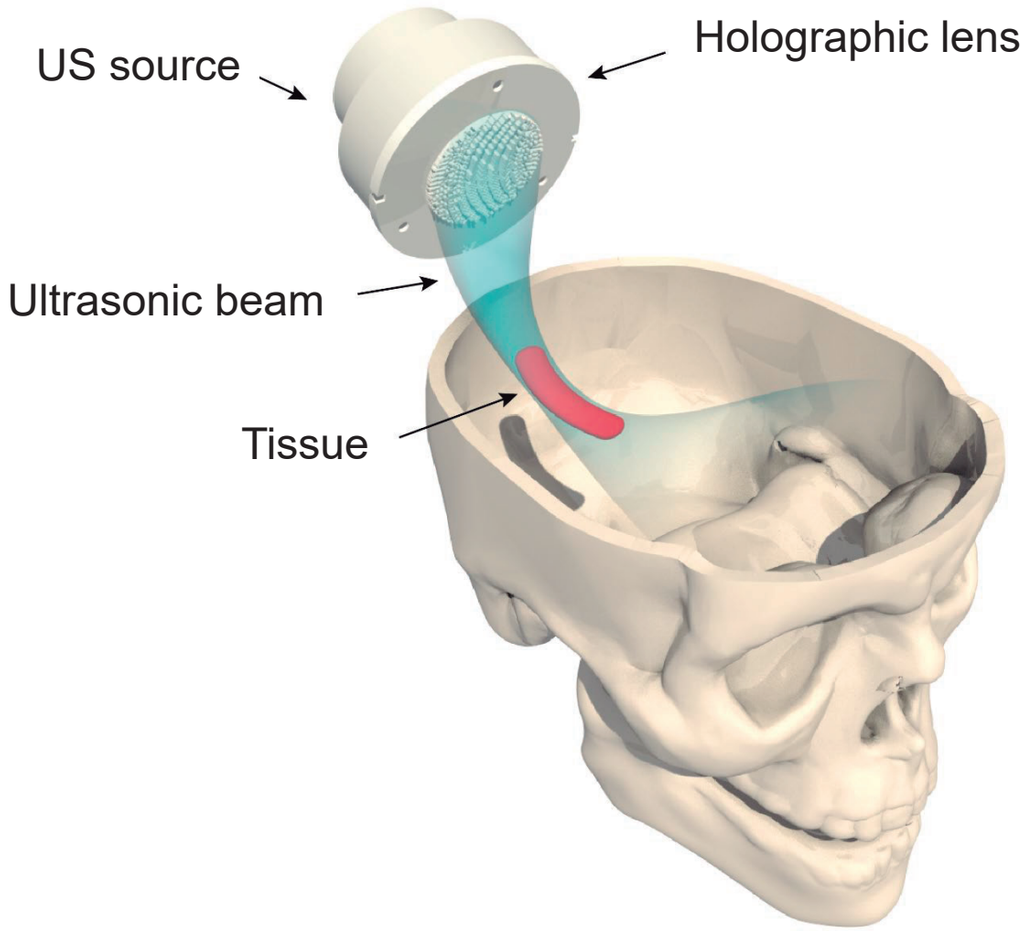
→

- Several sonications are needed.
- Or our proposal: a single holographic sonication.

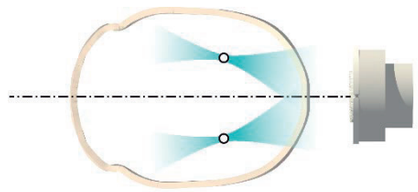




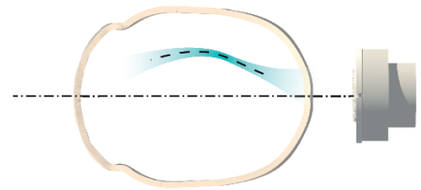
Hologram for the brain



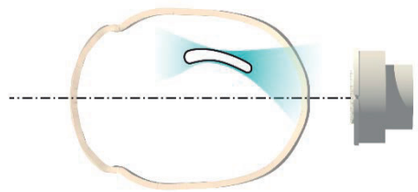
1. Multiple focusing



2. Self-bending beams

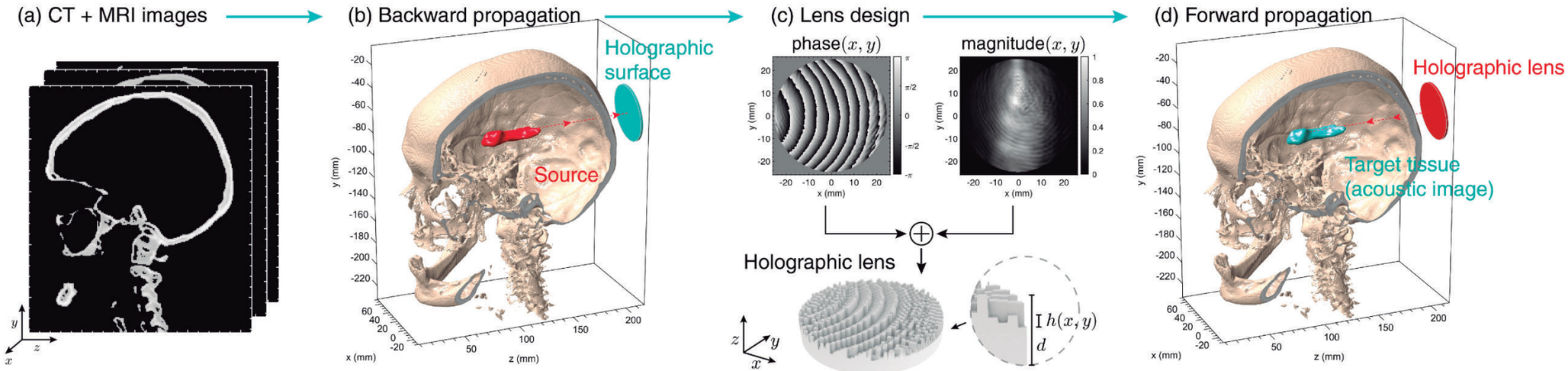


3. Holograms



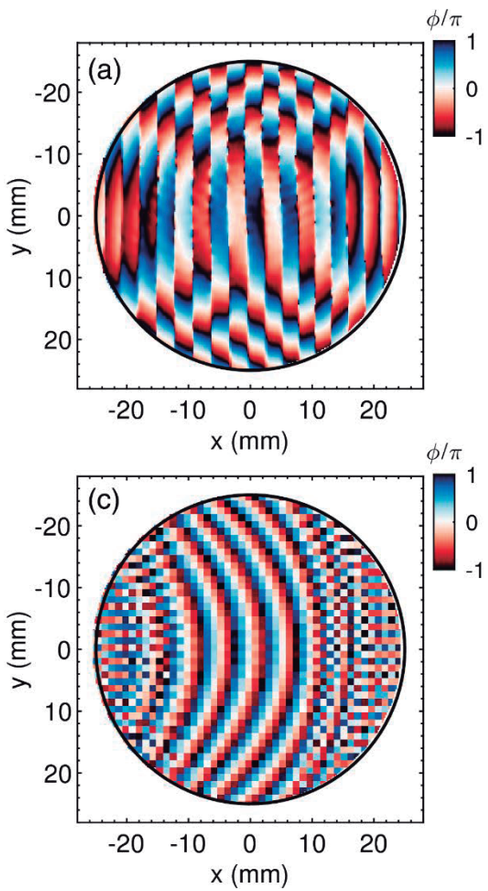
Hologram for the brain

- Protocol:
  1. CT (skull) + MRI (soft tissue)
  2. Time-reversal (phase conjugation)
  3. Lens design + 3D-printer
  4. Treatment

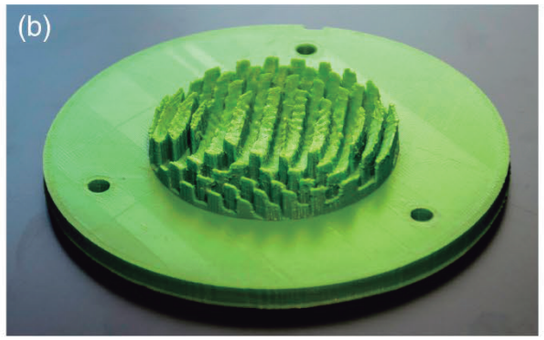


Hologram for the brain

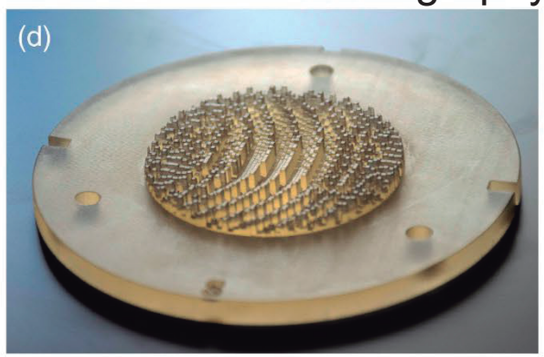
- Lenses example:

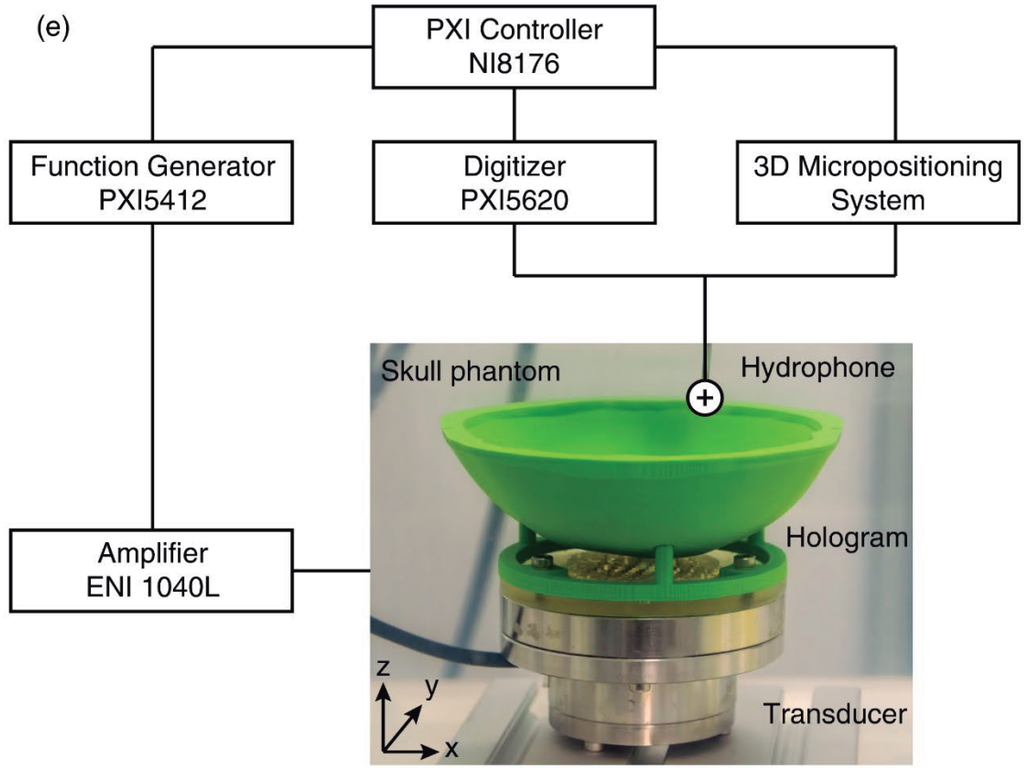


PLA



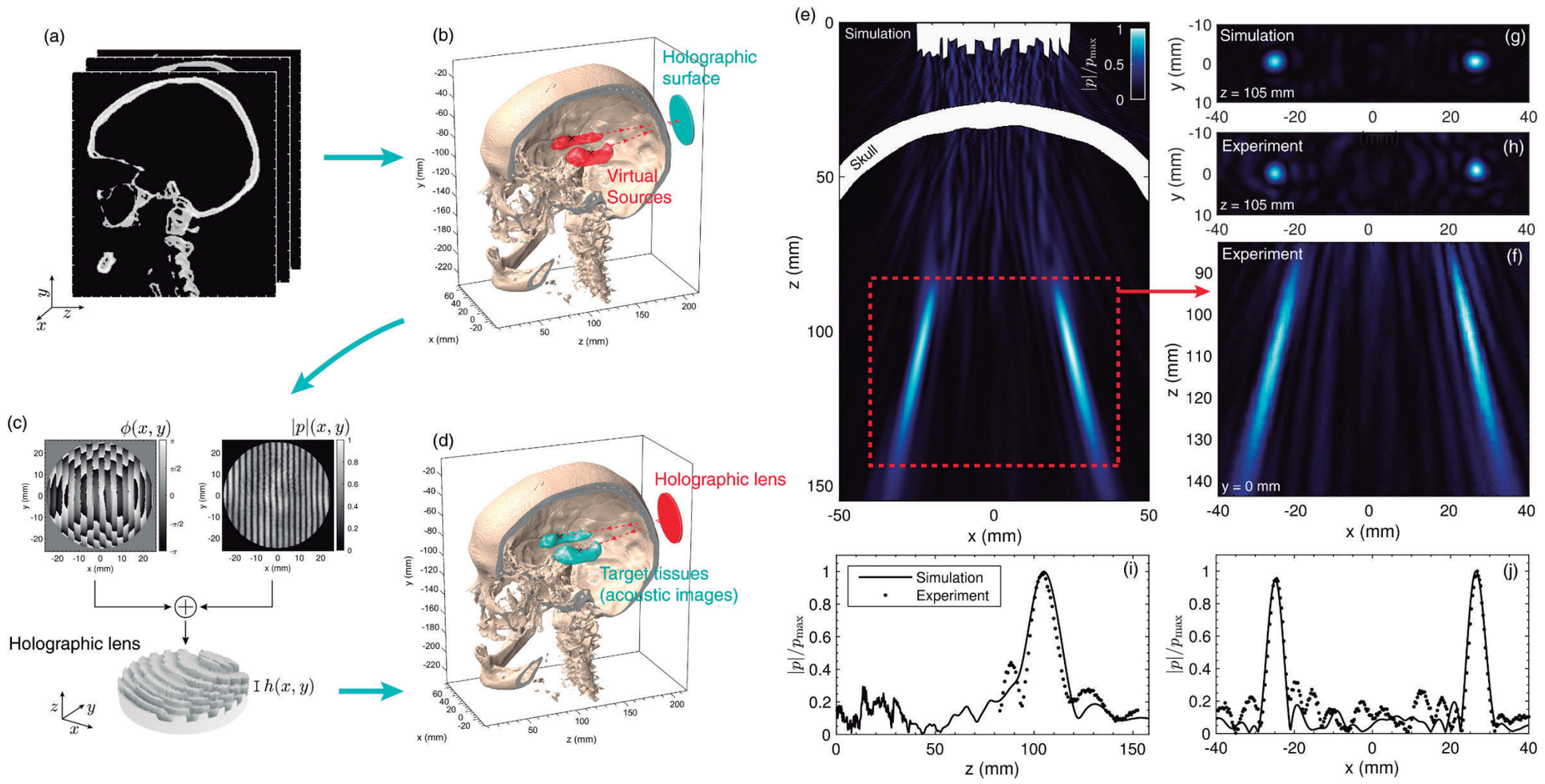
Estereolitography





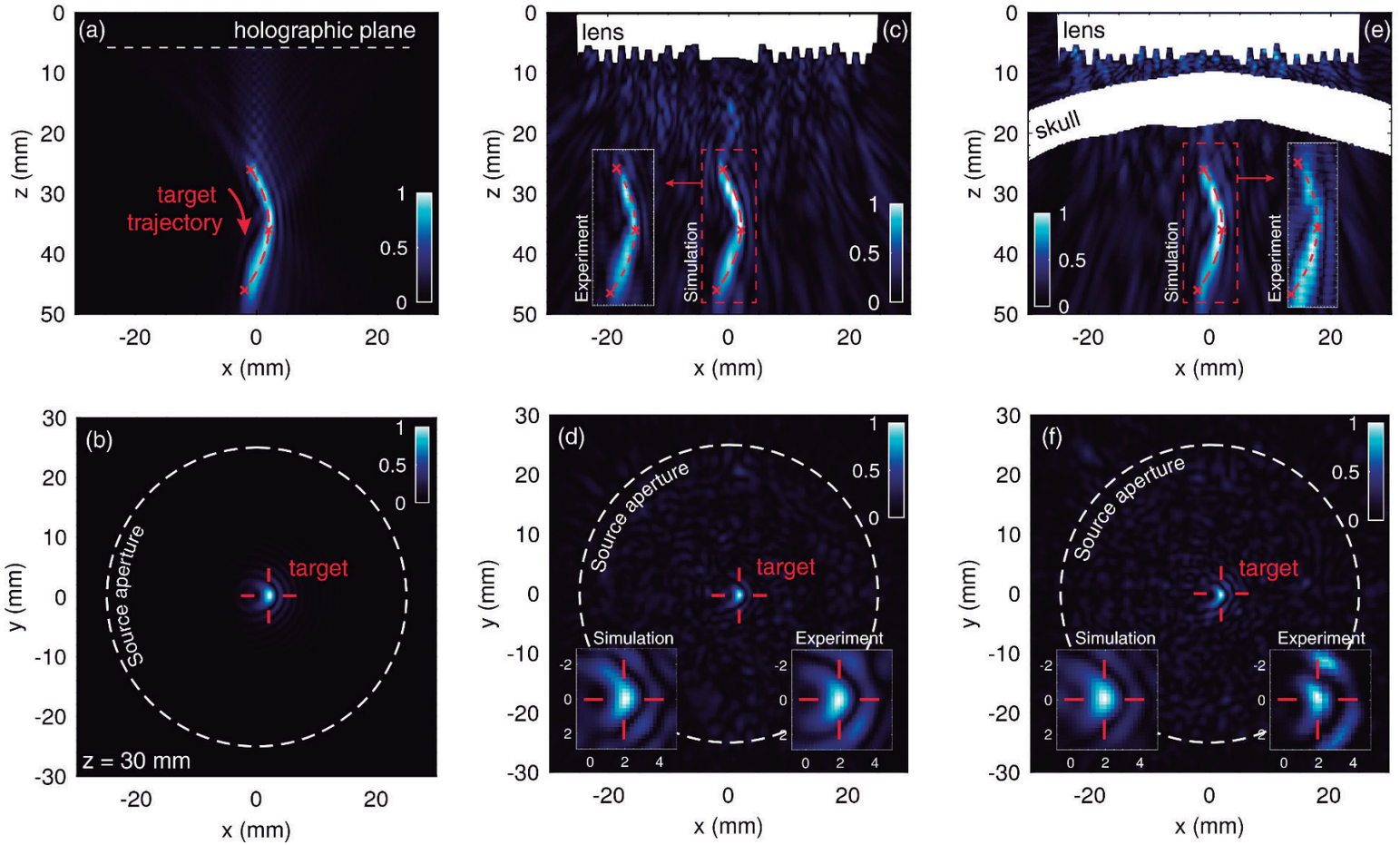
Hologram for the brain

1. Multiple focusing



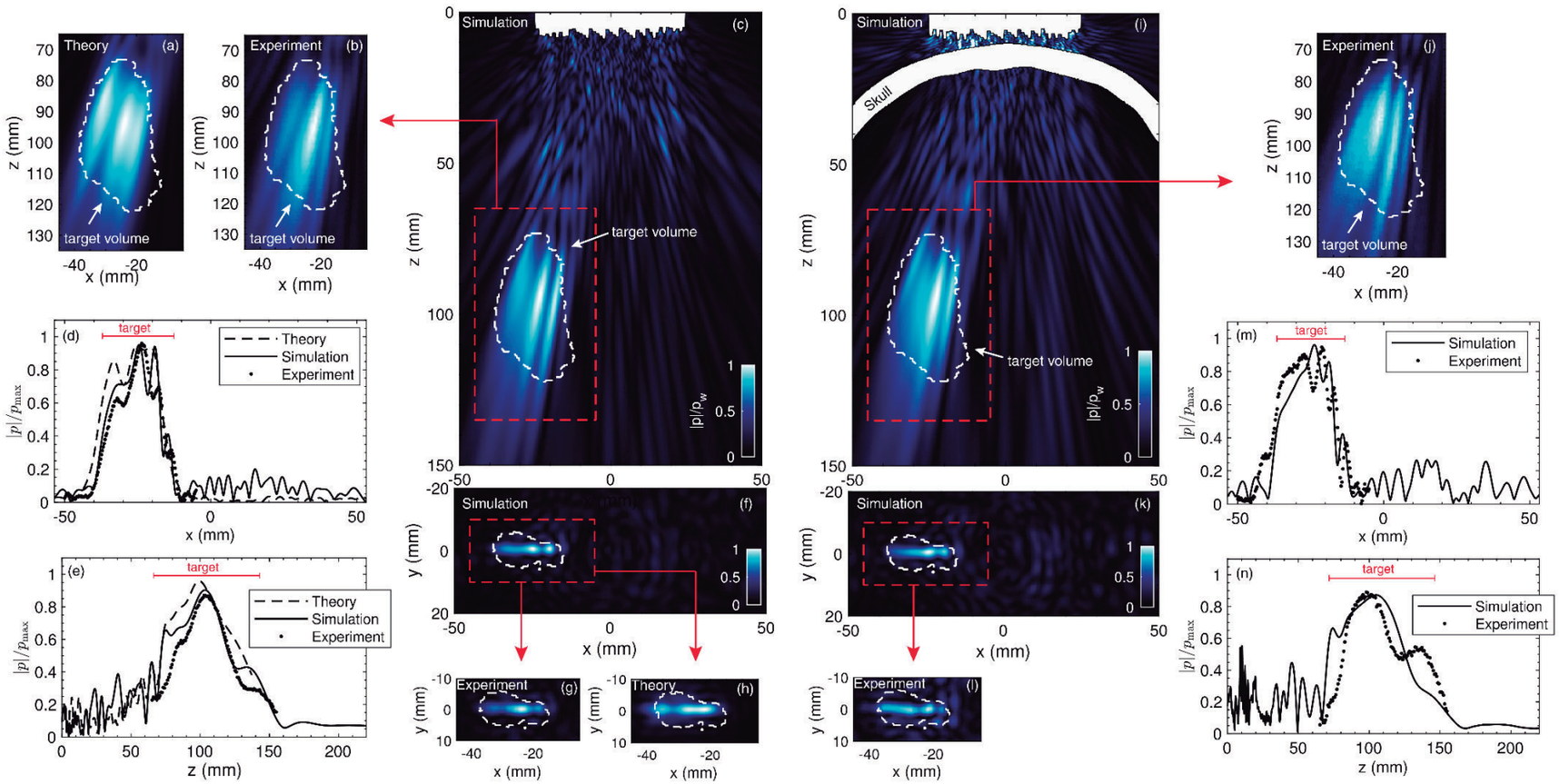
Hologram for the brain

1. Self-bending beams



Hologram for the brain

Volumetric holograms (diffraction limited)



Conclusions

Focused ultrasound

- Terapia no ionizante,
- No invasivo,
- Post operatorio reducido

Limitaciones

- El ultrasonido es una onda, sufre de difracción /atenuación / refracción
- Control sub-milimétrico de la focalización tiempo real
- Calentamiento del cráneo el tratamientos de ablación

Aplicaciones específicas

- Amplio abanico de aplicaciones y posibilidades
- Aplicaciones emergentes
- Ensayos clínicos prometedores

Resultados

Publicaciones

1. N Jiménez, F Marquet, F Camarena, EE Konofagou, J Redondo, B Roig, R Picó.
   Estudio de la propagación no lineal de haces de ultrasonidos focalizados a través del cráneo
   Revista de Acústica, 43 (1), pp. 5-11, (2012)
2. N Jiménez, F Camarena, J Redondo, V Sánchez-Morcillo, Y Hou, EE Konofagou.
   Time-Domain Simulation of Ultrasound Propagation in a Tissue-Like Medium
   Acta Acustica united with Acustica, 102 (5), pp. 876–892, (2016)
3. N.Jiménez V Romero-García, L M. García-Raffi, F. Camarena, and K. Staliunas
   Sharp acoustic vortex focusing by Fresnel-spiral zone plates
   Applied Physics Letters 112, 204101 (2018)
4. S. Jiménez-Gambín, N. Jiménez, J.M. Benlloch, F. Camarena.
   Holograms in the brain: focusing arbitrary acoustic fields through aberration layers.
   Scientific Reports (Under review) (2018)
5. S. Jiménez-Gambín, N. Jiménez, J.M. Benlloch, F. Camarena.
   Focal aberrations of focused ultrasound fields generated by single-element transducer.
   (In preparation) (2019 expected)

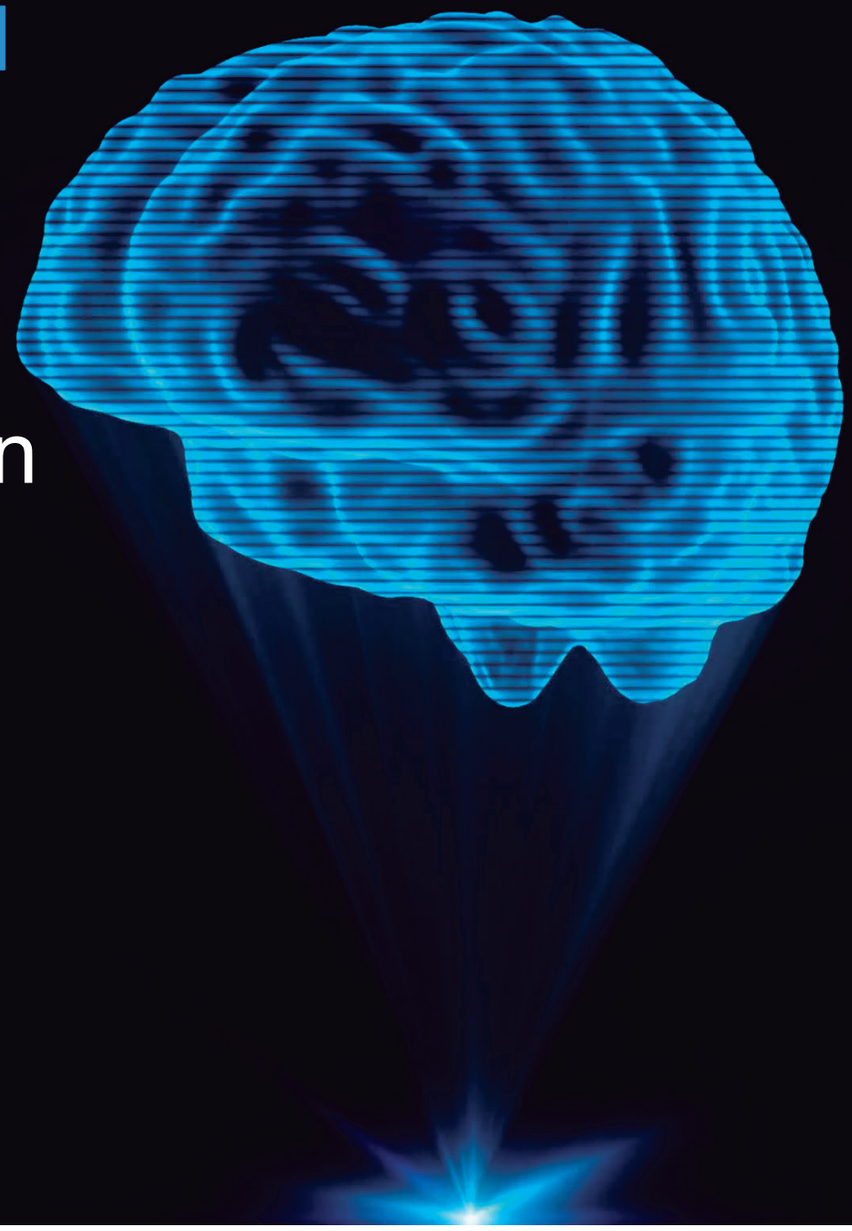
Patente solicitada

- Método de fabricación de una lente y dispositivo de ultrasonidos que comprende dicha lente (presentada y aprobada 2018)

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