

Focused Ultrasound
guided by
Magnetic Resonance Imaging

Eyal Zadicario

June 2016

INSIGHTTEC

COMPANY PROFILE

INSIGHTEC



INSIGHTEC is a privately held Israeli company founded in 1999



Developed ExAblate® - the first FDA approved therapeutic device using MR-guided Focused Ultrasound



~160 employees worldwide

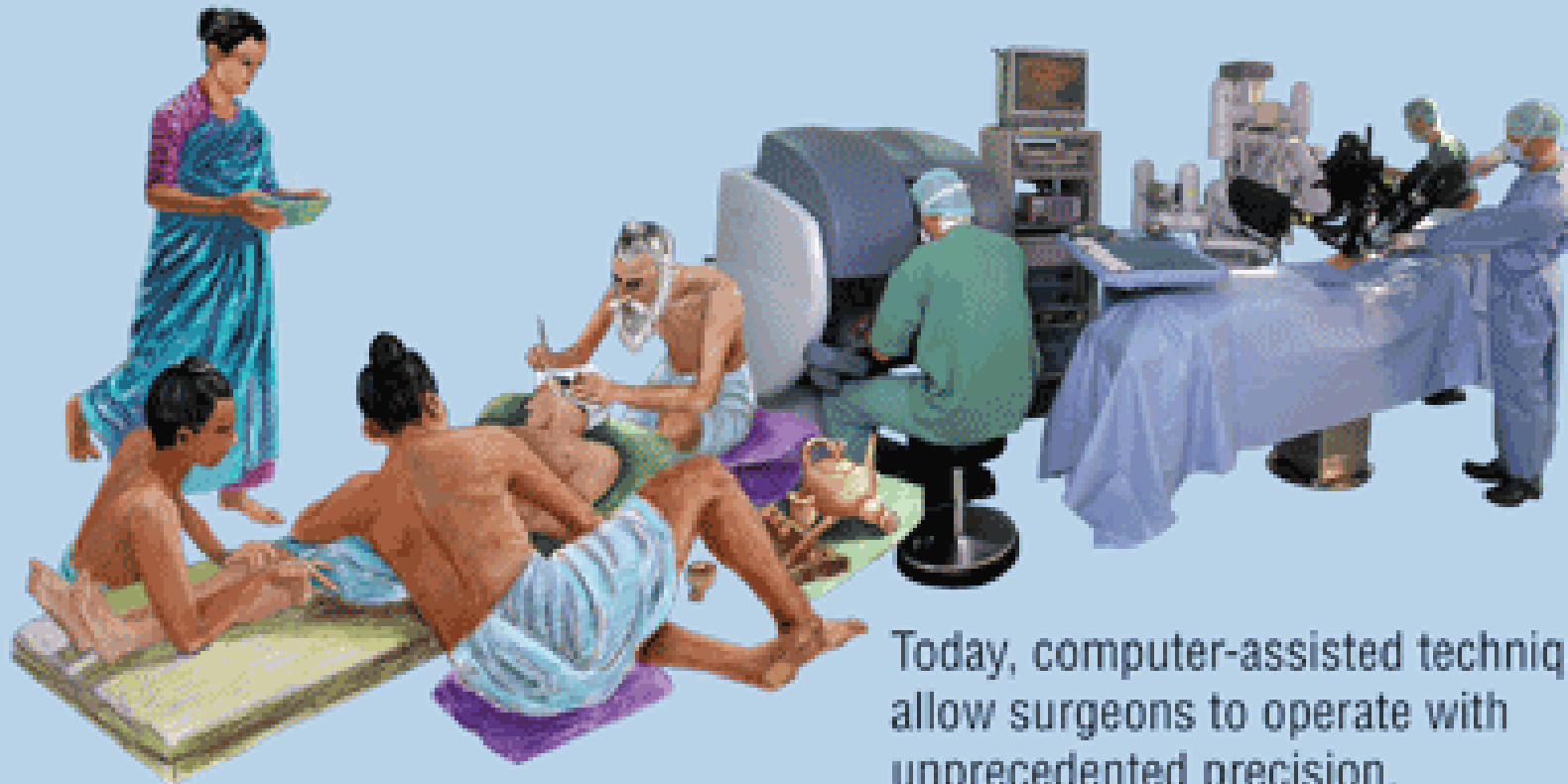


First to develop technology to successfully steer and focus ultrasound through the cranium

Headquartered in Haifa, Israel. Regional offices in US, China, Japan and Europe.

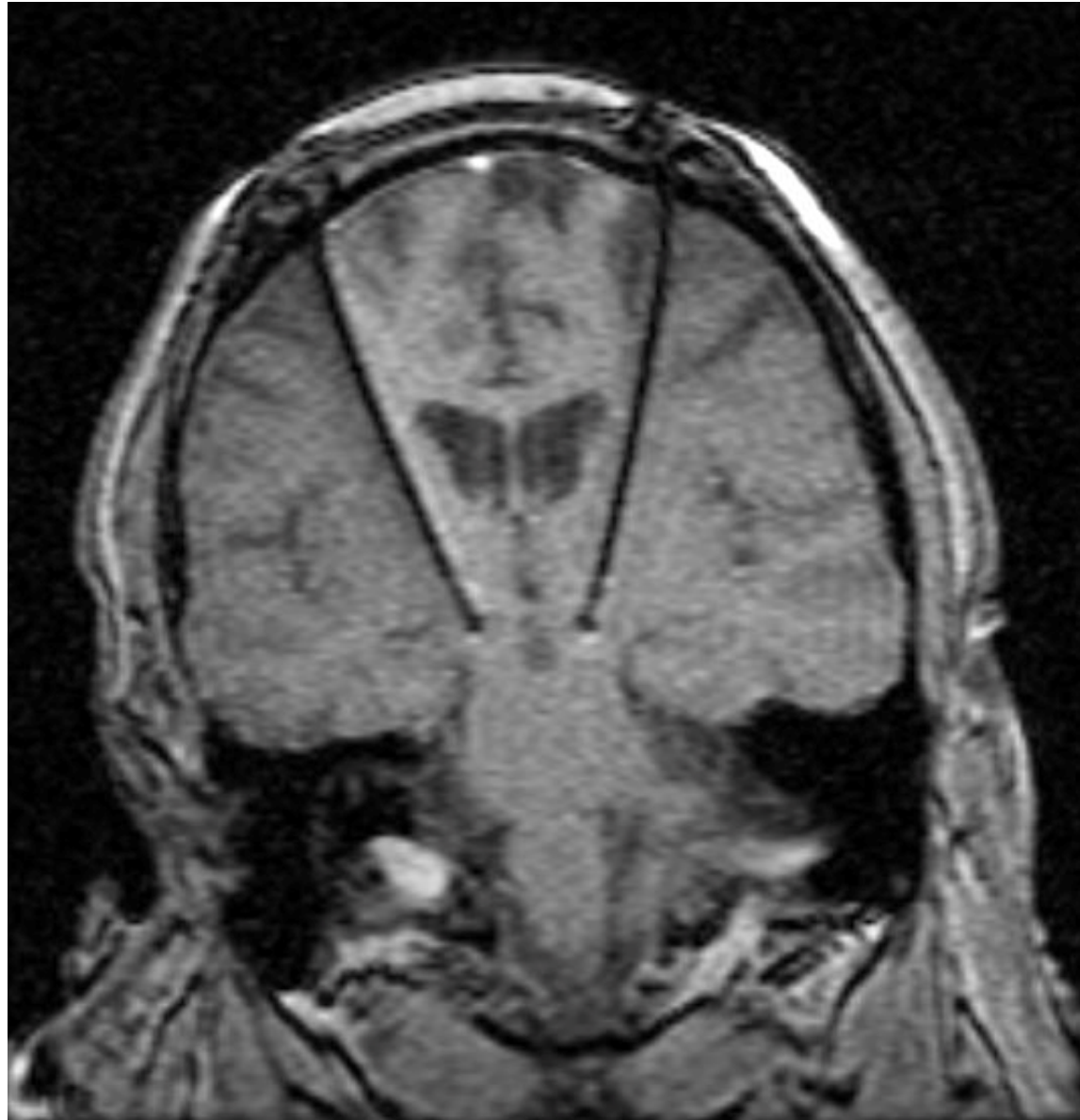
A 4,000-YEAR TRADITION AND TODAY'S INNOVATIONS

Ancient Hindus were the first known people to use surgery to remove tumors. By 2000 BC they had even developed reconstructive plastic surgery.



Today, computer-assisted techniques allow surgeons to operate with unprecedented precision.





INSIGHTEC

Acoustic surgery

The Non Invasive Surgery Room of The 21st Century



Body incision to remove the tumor



Minimal incision to remove the tumor



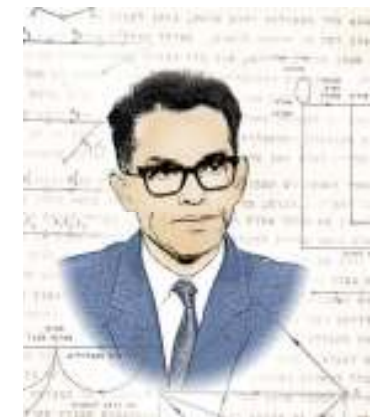
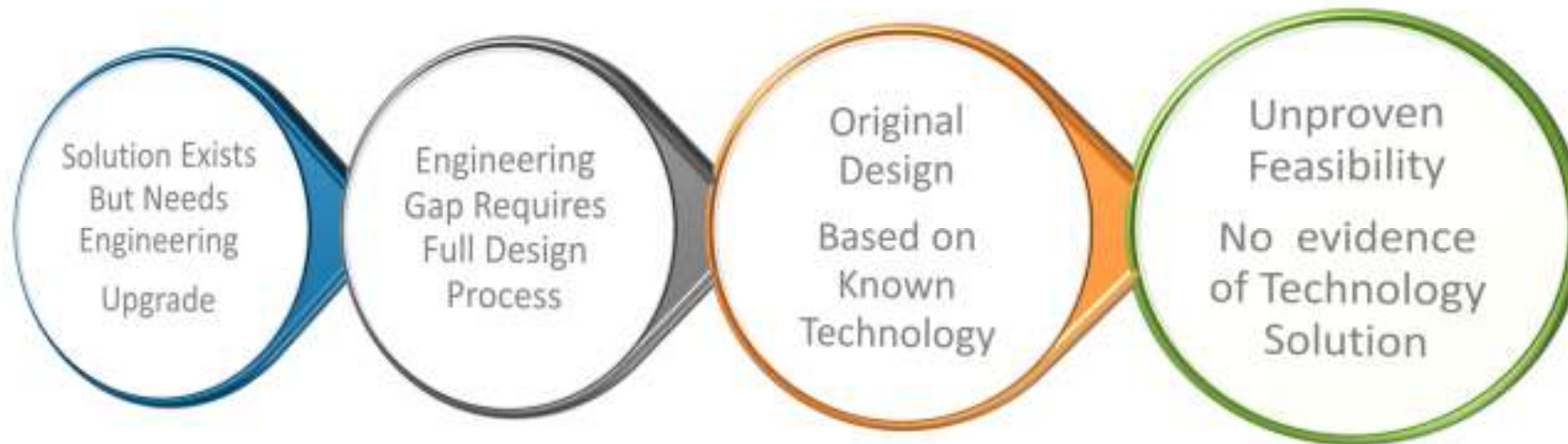
Non-invasive surgery





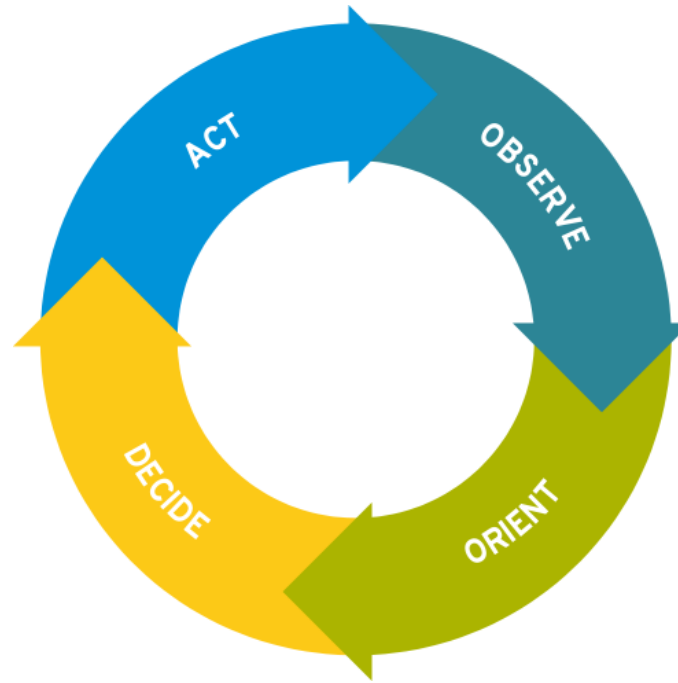
Technology

DEVELOPMENT KNOWLEDGE GAP & RISK ASSEMENT

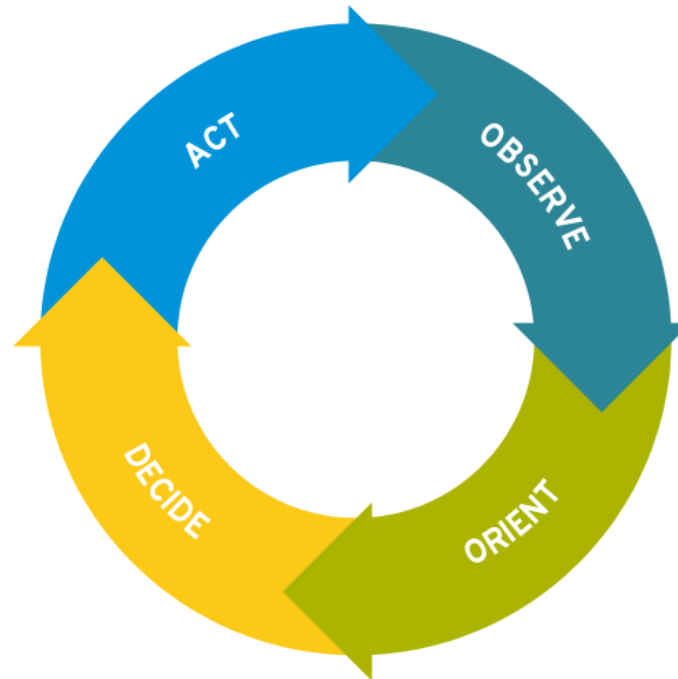


מס' רמה לפי בונן	הגדרה לפי בונן	תיאור מצב בשלות התכנן	הנדורה לפי P&B	רמה לפי TRL	דרישה לירידת הפער	סכבי פיתוח (לפי בונן)
1	פער עדכון	ידוע, נעשה אצלנו, נדרשים התאמה או עדכון	תכן וריאנט	9	הוכחת ייצור הדיר	1-1.5
2	פער הנדסי	ידוע מה צריך לעשות ומוכר אך דורש תהליך פתוח מלא	תכן התאמה	3-8	תיקוף (ולידציה) בפיתוח	2-3
3	יש רק משפט קיום	ידוע שניתן לפתור, טכנולוגיה קיימת אך לא ידועה. אף פעם לא נעשנו.	תכן מקורי	1-2	הדגמה בפיתוח	2-3+M
4	אין משפט קיום, דרוש מחקר	לא ידוע אם קיים פתרון או אם קיימת טכנולוגיה	-	-	הוכחה תיאורטית שקיים פיתרון, שמישהו עשה	+M ?+2-3

OODA LOOP



SURGERY



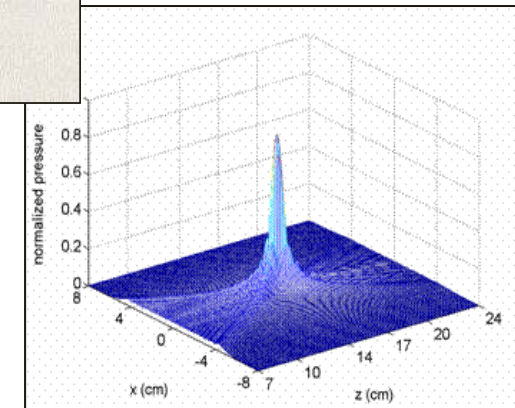
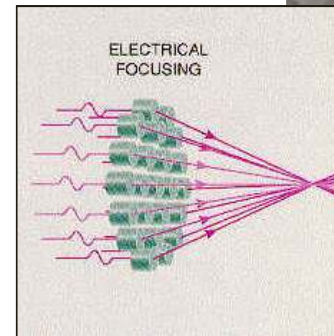
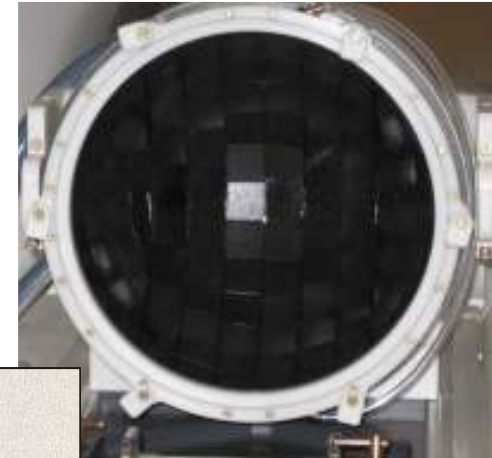
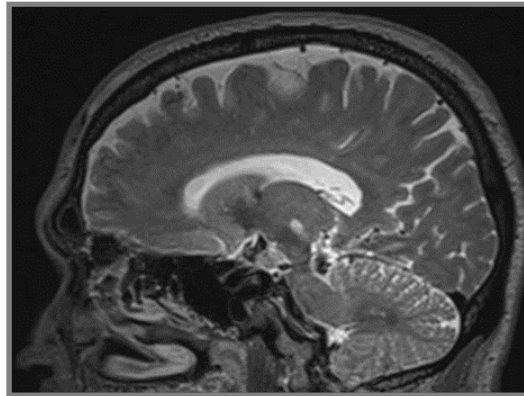
Guidance



Treat

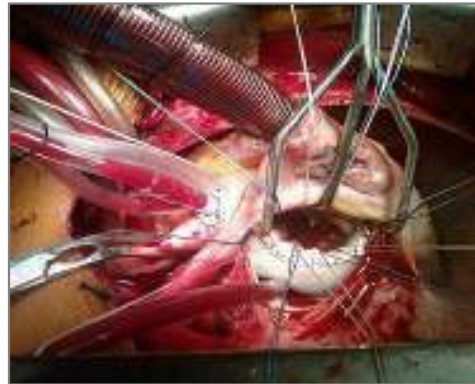


Real Time Feedback



ExAblate – MR guided Surgery

SURGERY



Guidance

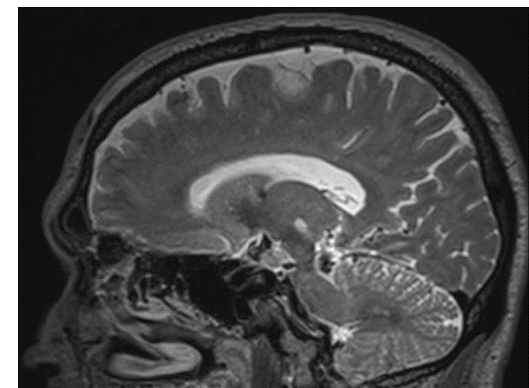
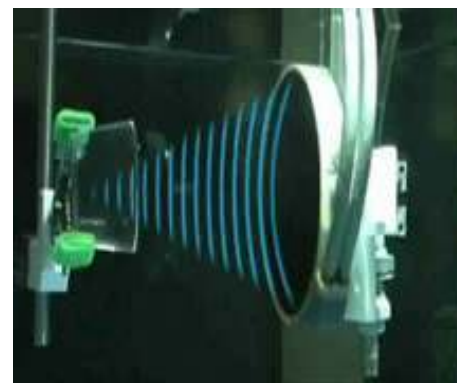
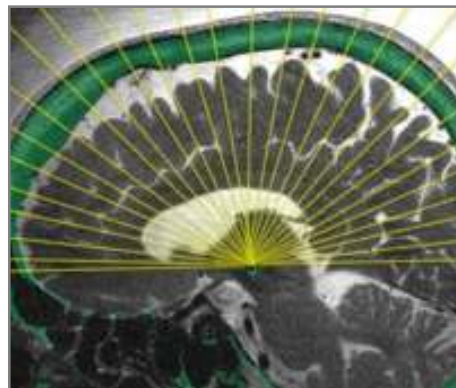


Treat



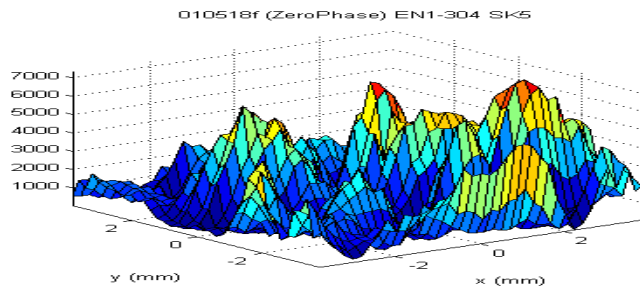
Real Time Feedback

Acoustic
Surgery

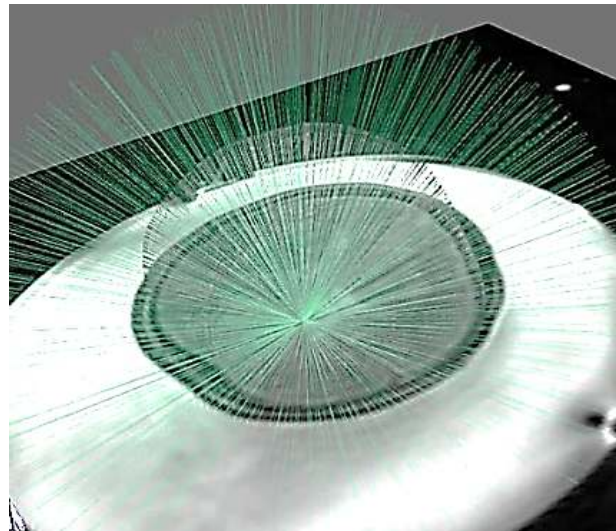




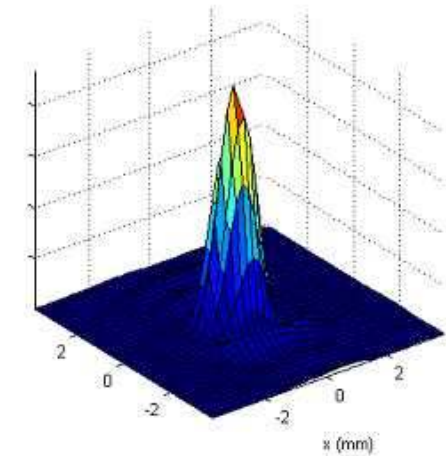
A ONE OF A KIND TECHNOLOGY FOR INCISION LESS TREATMENT OF THE BRAIN



Natural Ultrasound
De-Focusing by the Skull



Unique through skull
Focusing Technology



Corrected Ultrasound
Focusing through Skull

Acoustic Surgery in Neurosurgery

Transcranial Barriers

- Absorbs Ultrasound Energy
- Skull Variability
- Non Homogenous

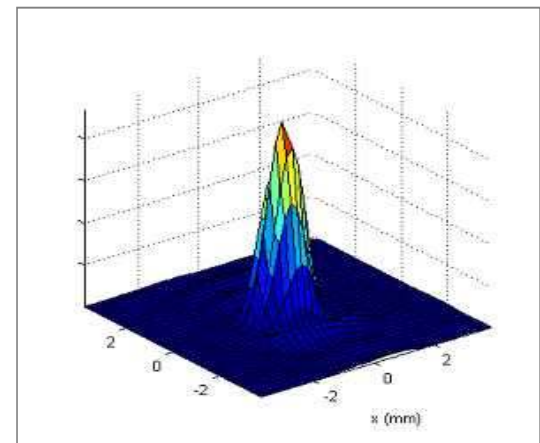
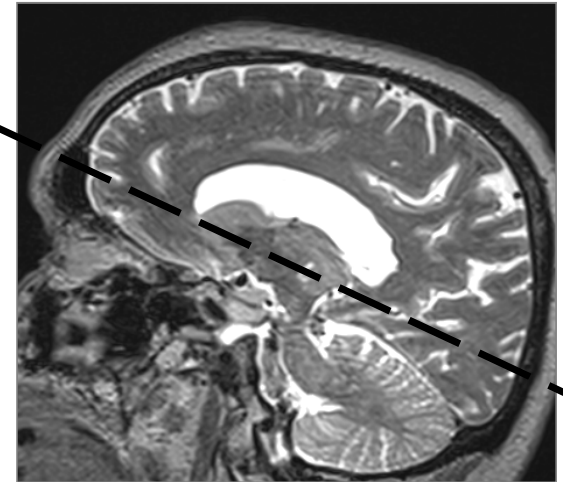
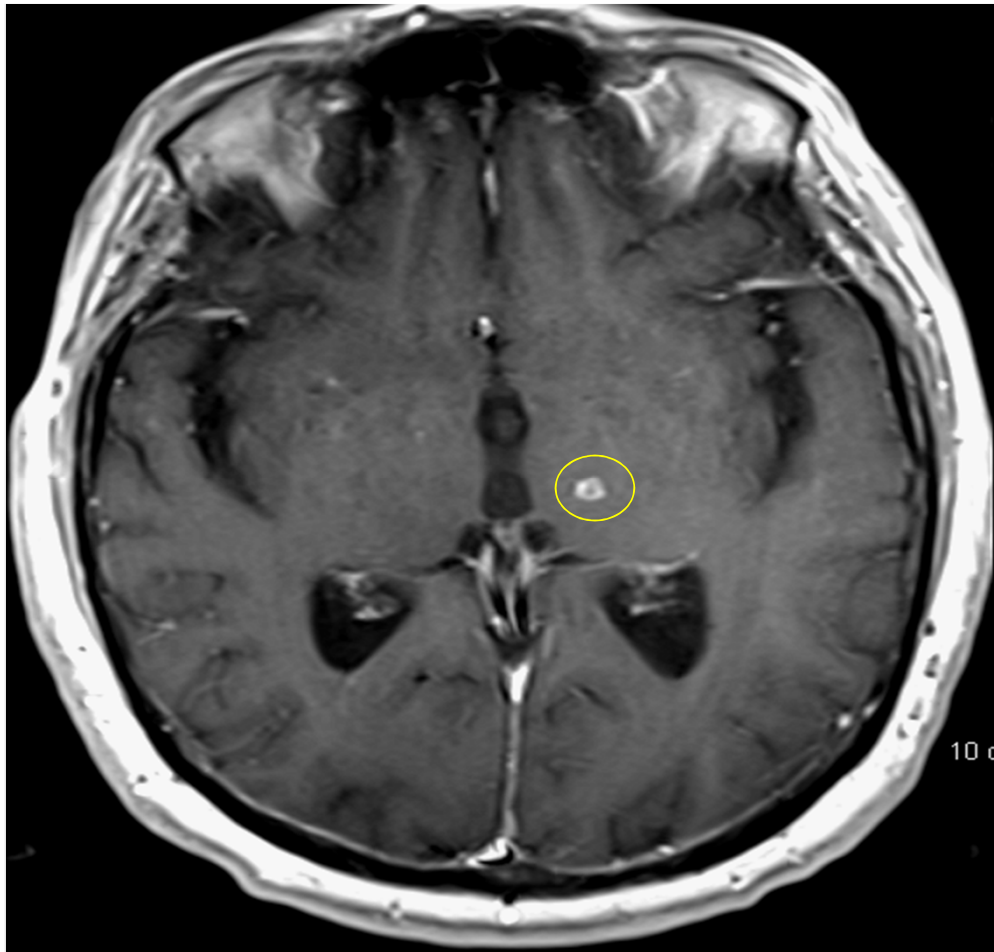
Focused Ultrasound Technology

- High Power Ultrasound
- Phased Array Technology
- Personalized Acoustic Beam



INSIGHTEC

IMMEDIATE POST TREATMENT EFFECTS





Products

3 PRODUCT
FAMILIES

INSIGHTEC
Therapy In Focus

NEUROSURGERY

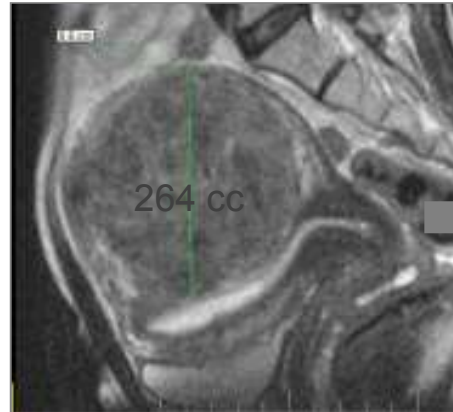
ONCOLOGY

WOMAN'S
HEALTH

INSIGHTEC

UTERINE FIBROIDS/ MYOMA

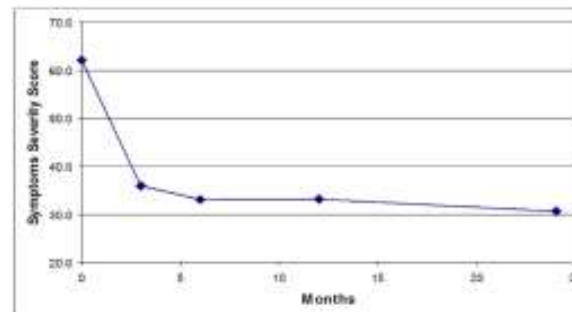
- Fibroids affect ~70% of women above 30, 25% of them will suffer from symptoms.
- Current standard of treatment is hysterectomy
- Over 12,000 women have been treated
- Worldwide regulatory approval



T2W image before treatment, after 3 months GnRH



T2w contrast image 12 months post MRgFUS treatment



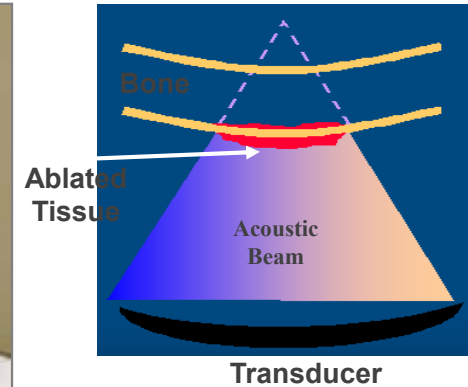
Measured mean Symptoms Severity Score of Quality of Life scale after ExAblate treatment



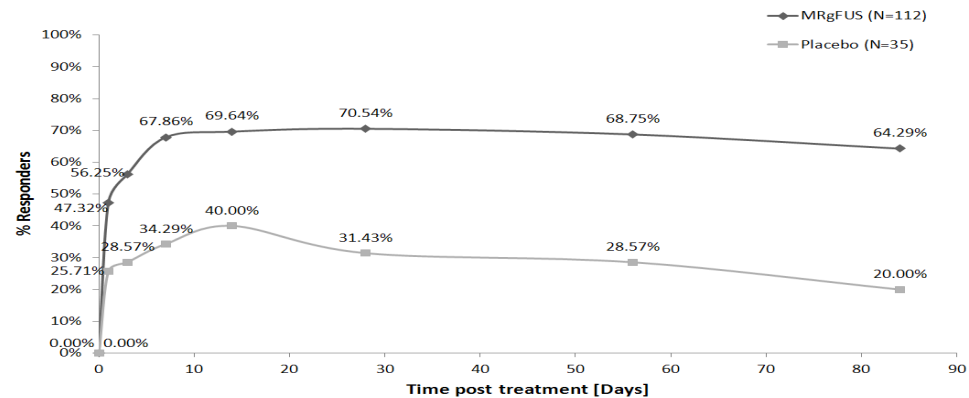
Courtesy of W. Gedroyc, Saint Mary's London, UK

BONE METASTASES

- 76 % of patients with bone metastases reported moderate to severe bone pain at some point in their disease pain relief
- Current standard of treatment is EBRT. 35% of treated patients do not experience pain relief
- 660 bone tumor patients have been treated
- FDA & CE approval for pain palliation of bone metastases. CE approval for benign bone tumors



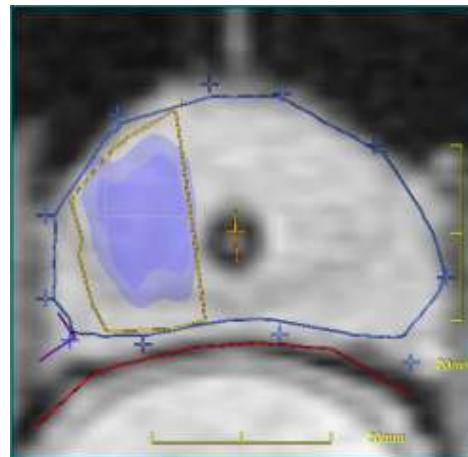
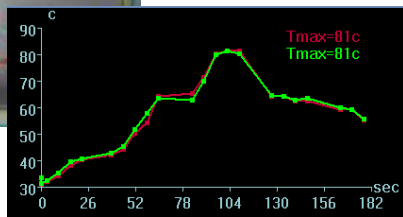
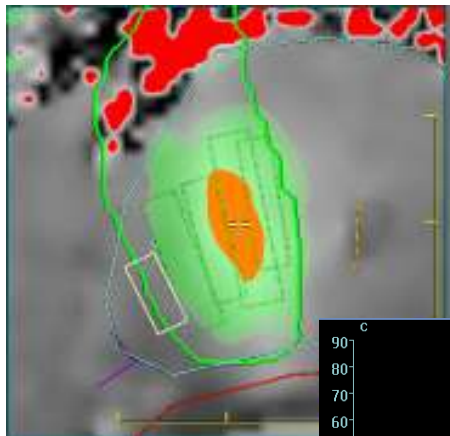
Treatment Response Rate N=147 RCT



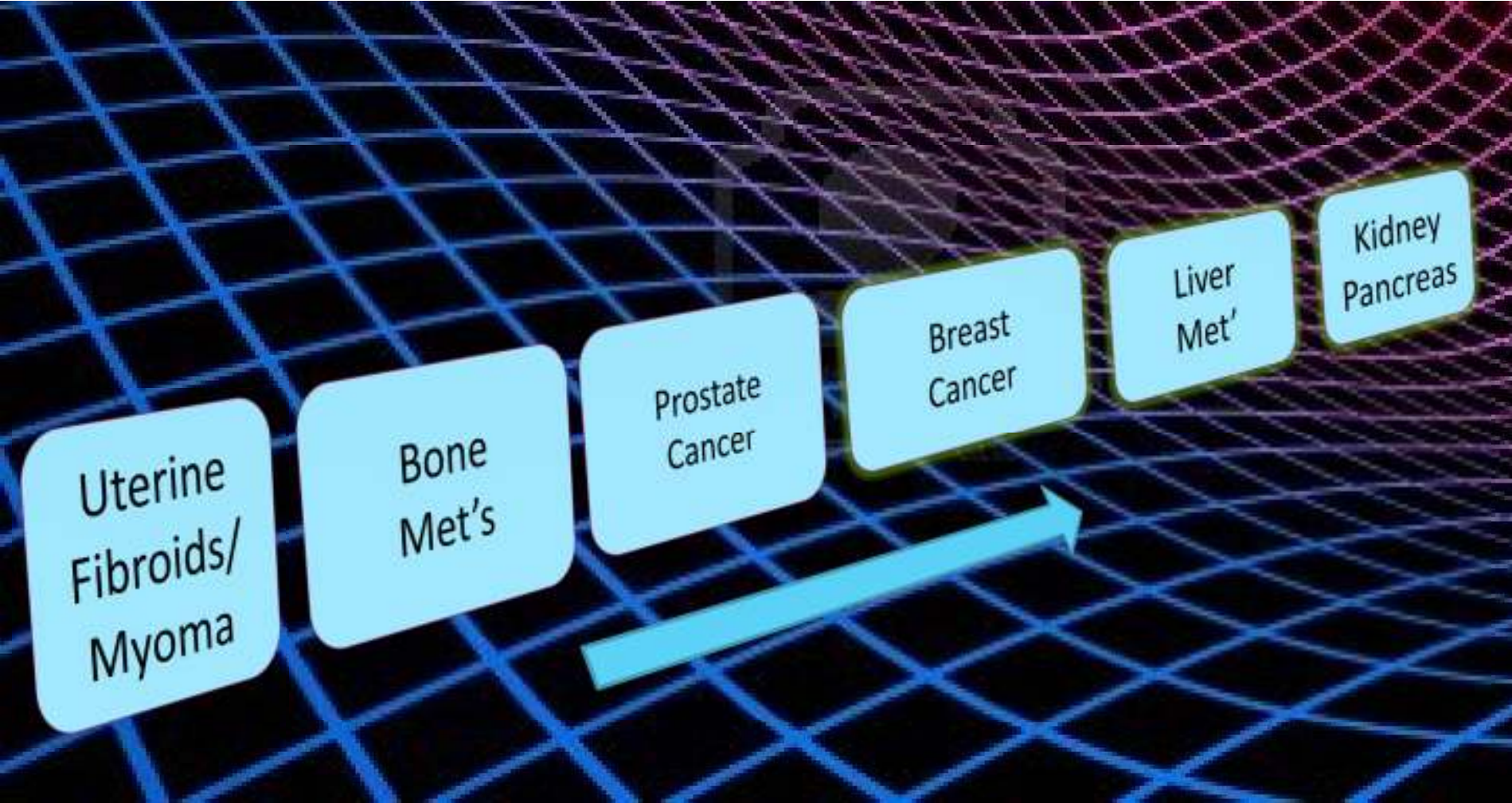
Main results of RTC trial: N=147:
 2/3 of responses seen within 3 days in 1 session.
 47% of treated patients reduced or completely stopped MEDD

•Hurwitz, et al., *Magnetic Resonance-Guided Focused Ultrasound for Patients With Painful Bone Metastases: Phase III Trial Results*, Oxford Journals Medicine JNCI Journal of the National Cancer Institute, March 2014

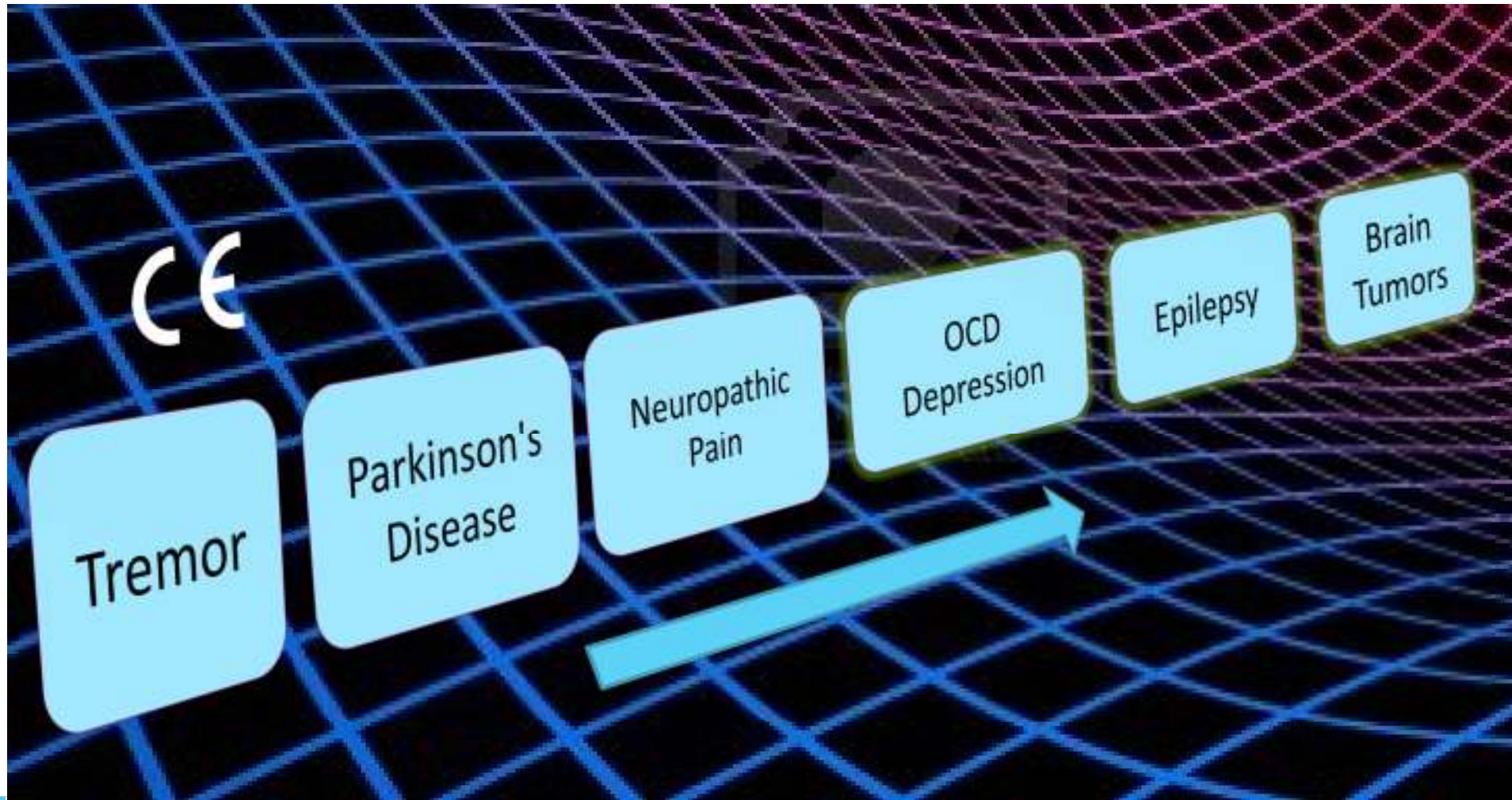
PROSTATE ABLATION



EXABLATE – ACOUSTIC SURGERY ROADMAP



EXABLATE NEURO - THE ROADMAP BEYOND TREMOR





Future Research

FIRST HUMAN BBB PROOF OF CONCEPT

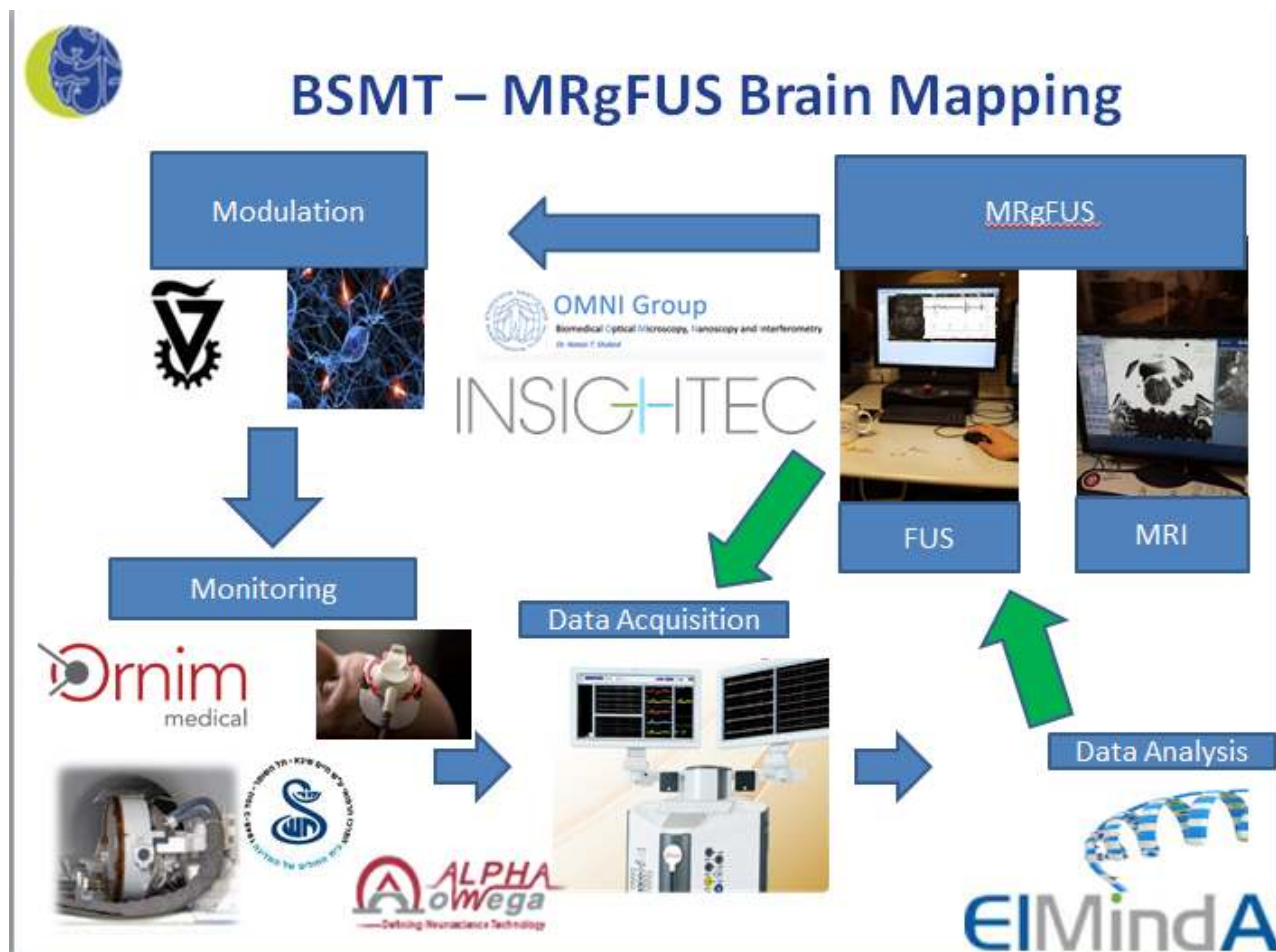


Uptake of gadolinium following microbubble injection and scanning ultrasound beam in 3x3 pattern showing very selective uptake due to BBB opening in that same pattern

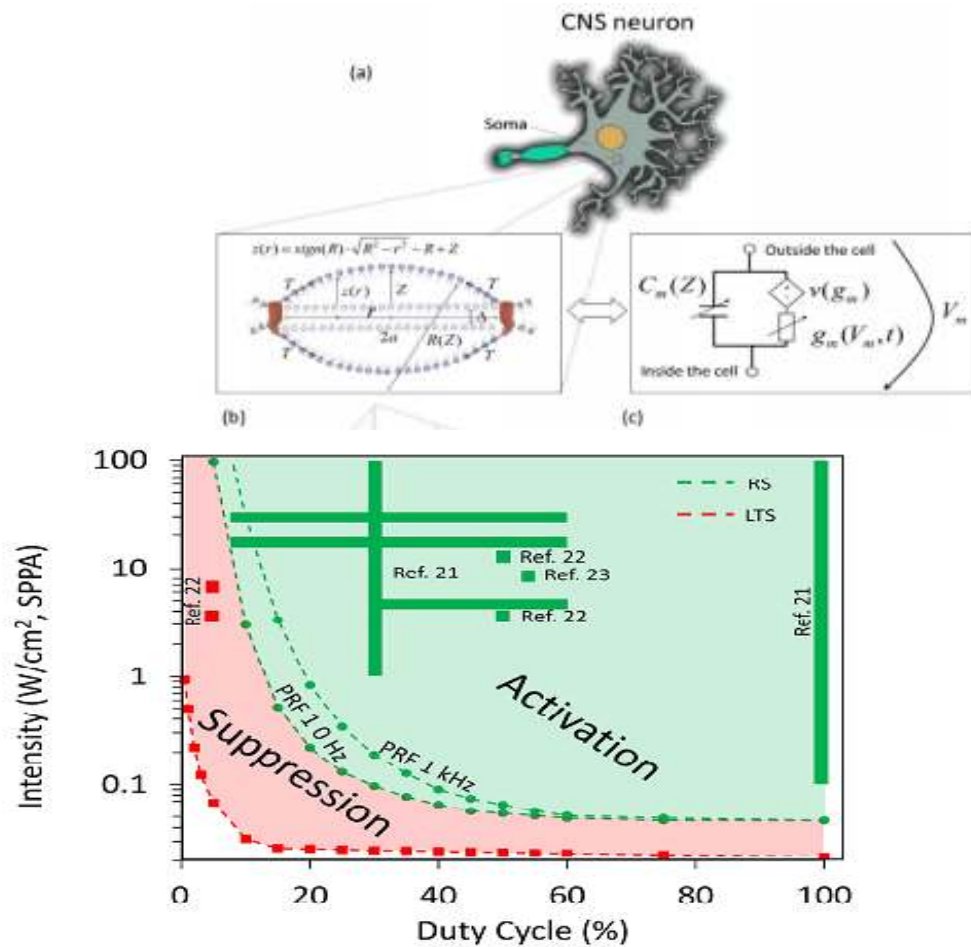
Todd Mainprize MD
Sunnybrook Health Science Center
Toronto, Ontario

CTV News November 8, 2015

COLLABORATION PROGRAMS



Kimmel's biophysical model



In-vivo neurostimulation

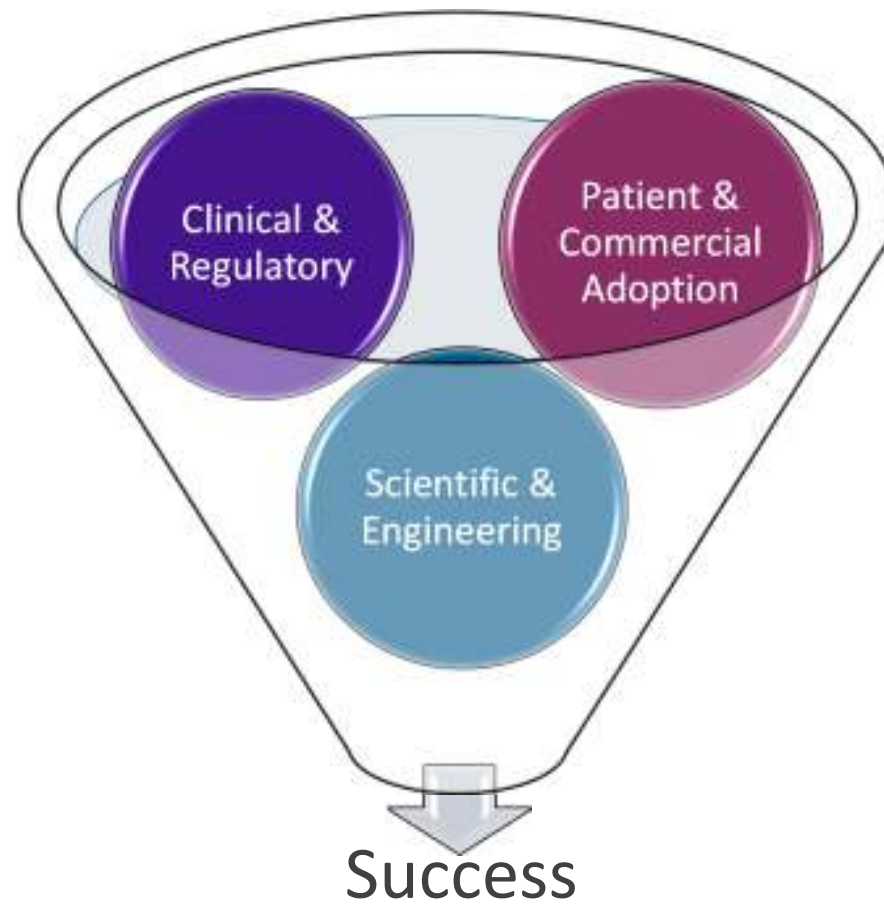


Courtesy of Michael Plaksin, Shy Shoham and Eitan Kimmel
 King R et al. Effective parameters for ultrasound-induced in vivo neurostimulation.
 Ultrasound in Med and Biol 2013



The Challenge

WHAT ARE THE CHALLENGES



SCIENTIFIC & ENGINEERING CHALLENGE

- Physics transducer technology
- Multiple element phased array [>1000 elements]
- High power driving electronics in MRI RF environment
- MR compatible robotics
- Software algorithms and thermo-acoustic simulations
- Image processing Visualization and clinical user interface systems
- Acoustic feedback systems
- Therapy Specific MR imaging techniques
- Complex Device integration with MRI

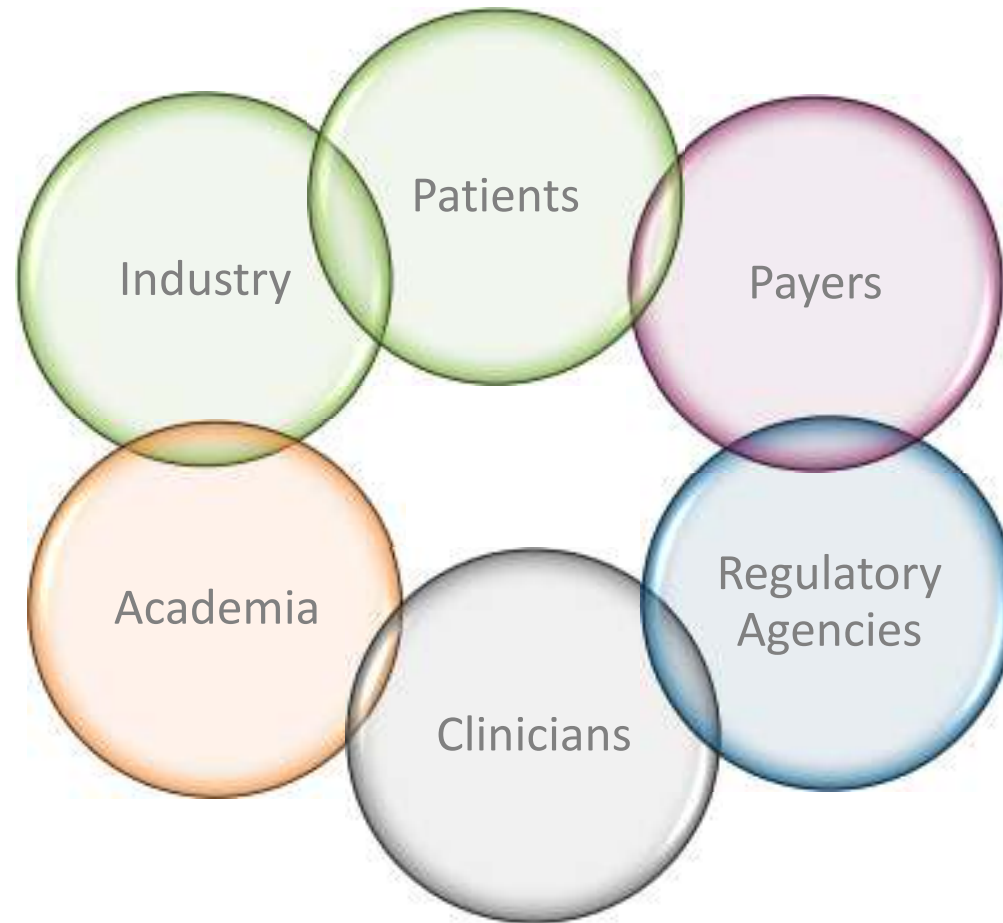
CLINICAL & REGULATORY CHALLENGE

- Novel Modality investigated thoroughly
- No predicate in the market
- Education of regulatory agencies
- Clinical trials to support safety and efficacy
- Multinational diversity

ADOPTION CHALLENGES

- Patient awareness and compelling need
- Clinical acceptance by medical societies
- Workflow and patient pathways
- Payers and reimbursement

MULTIDIMENSIONAL COLLABORATION





The Benefit

“Put Technology Where It Matters Most.....”





INSIGH+ITEC