Sofaer International Case Competition 2014

The Quest for ROI –

Return On Imagination

InSightec - The Quest for ROI – Return On Imagination

The operating room of the future: Opportunities and challenges

Imagine an operating room where tumors are removed, neurological dysfunctions corrected and illnesses or their symptoms are relieved without a single incision of the scalpel, no blood is drawn, and what's more, patients usually return home immediately after the procedure without a single day of hospitalization. Most people would consider such a scenario science fiction. However, this reality is already happening in dozens of hospitals and outpatient clinics around the globe, from the US in the west to Korea and Japan in the east.

InSightec, an innovative Israeli medical device company headquartered just outside Haifa, is perhaps the best kept secret of the medical world. A pioneer in the field of focused ultrasound (FUS) treatments, its literally cutting edge technology has the potential to revolutionize the way we think about surgery, neuroscience and interventional medicine. Despite its innovative technology, proven record and undisputable reputation, InSightec has not yet been able to transform its potential into full economic success. The company's management is seeking to radically change its business outcomes and recoup its immense R&D outlay in the near future.

From surgery to non-invasive, disruptive technologies in an ancient profession

(Exhibits 1-6)

Surgery is a closed process of adaptive, real time decisions being made by a single person, or a very small team of professionals. In this sense at least it is perhaps one of the few fields in medicine that has changed very little over the past centuries, or even millennia. In general, the surgical process involves cutting through healthy tissue in order to reach and treat a damaged

Udi Aharoni from the Eli Hurvitz Institute of Strategic Management at the Recanati Business School, Tel Aviv University, prepared this case with the assistance of Erez Cohn, Alon Epstein and Shira Lifshiz as the basis for a case competition. The case does not intend to illustrate effective or ineffective handling of business processes or decisions.

organ or area. It is an extremely focused process on the one hand, but inflicts minor to significant collateral damage on the other. The medical community and patients alike dream of technologies that can accomplish the feats of surgery, without its drawbacks, and the scientific community is indeed making strides in this direction. FUS is one of the few truly non-invasive technologies, allowing doctors to treat an affliction deep within the body, without drawing a single drop of blood.

FUS has been around for decades. Discovered during the 1940s by Lars Leksell and the Fry brothers, its potential was apparent, but it was abandoned due to lack of the supportive technologies that would enable monitoring of treated areas and deliver real-time feedback. Not to be discouraged, Leksell went on to invent the Gamma Knife, another non-invasive surgical procedure, which utilizes radiation to treat the afflicted areas.

FUS made its comeback with the invention and development of imaging systems – ultrasound (US) and magnetic resonance imaging (MRI). MRI allows the physician to receive real-time feedback through a set of critical parameters, including location, temperature mapping, and movement. FUS is basically an acoustic beam that generates oscillation, friction and heat, destroying cells through protein and capillary denaturation; a process called ablation. The acoustic beam is highly focused, causing damage only at the point where it is aimed, and leaving all the surrounding tissue unharmed. Treated cells reach temperatures of 65°C–80°C, ensuring complete ablation. But how do physicians know exactly where to aim? And how do they know when the cell has been completely destroyed, and thus stop the ablation process? This is where MRI kicks in. The most advanced FUS technologies rely on magnetic resonance (MR) guidance, creating MRgFUS.

InSightec pioneered MRgFUS. It developed an apparatus built on existing MRI beds, adding FUS transducers that can be applied to body, limb and brain, to treat and even cure various conditions. A rival, but limited, technology exists, in which FUS is guided by ultrasound systems. This technology is being used for several indications by Chinese companies, and some western companies have pioneered its use mainly to treat prostate tumors. However, none of these companies have yet obtained FDA approval. The chief limitations of ultrasound guidance are the lack of precise visualization and the inability to provide thermal feedback.

The FUS technology is now at the point where it has the potential to effectively treat almost all parts of the body.

Revolutionizing the way healthcare is practiced and delivered

The non-invasive nature of FUS and the way it is applied give it the potential to change the way we think about healthcare delivery in general and revolutionize the very essence of the medical profession. The introduction of high-tech procedures that mediate the direct contact between the surgeon and the patient, the enhanced safety of these procedures, and the radically different approach to real-time decision making, have changed the medical learning curve. Non-invasive high-tech medicine presents a great threat to the classic order of things, in which novices train and practice medicine under the masters, who refine their techniques and knowledge over decades of practice. For one, the younger are more tech savvy, open to new ideas and more inclined to adopt innovative procedures. Having said that, the adoption of disruptive and innovative tools and procedures is not only a question of age, but rather the inclination to take risks, and having an inquisitive mindset. Early adopters are scarcer than those who stagnate, who choose to maintain the current status quo, with which they are most familiar.

Apart from the personal and generational threat that these procedures pose, the concept of ownership and the monopolies of certain medical vocations are threatened too. If traditionally invasive procedure were performed by surgeons, or specialty specific professionals, in non-invasive procedures in general and FUS in particular, radiologists have become the pivotal axes. Despite the fact that radiologists are never the primary caregivers (i.e. the patients are not theirs), they are the ones who own and master the performed procedures. However, technology ownership in the case of FUS is not straightforward. If interventional radiologists are clearly identified as owners (since they are traditionally early adaptors and are also part of the radiology departments) there are potentially three other categories of players: gynecologists for the uterine procedures, neurosurgeons for the brain solutions and radiation oncologists for the oncology line. For gynecologists, it would require a new mindset – not directly operating by hand but mediating through a device, something that started with the use of surgical robots such as the Da Vinci, in addition to investment in high CAPEX (capital expenditure) equipment. The neurosurgeons and radiation oncologists are already used to treating tumors with

irradiating techniques, such as the Gamma Knife or various linear accelerators which are high CAPEX equipment.

Not only does FUS have the potential to cause shifts within and between medical professions, but it also raises the question of the venues where healthcare is delivered. Today, most surgical procedures are still performed in hospitals, where the patient stays at least overnight. MRgFUS is typically an ambulatory, outpatient procedure, after which the patient goes home. Ambulatory procedures require less staff, no investment in dedicated operation rooms, and no cost expenditure for post-procedure hospitalization. The cost reduction which goes along with ambulatory care is seen as a major opportunity for healthcare insurers and providers.

Entry barriers

The market's entry barriers are very high and arise from a large number of sources and environmental conditions. First of all, there is the huge investment and long time spent in research and development (R&D). According to Blue Cross Blue Shield it takes 17 years for a new medical technology to be adopted, most of it being spent on R&D. Second, the market needs to be educated or even created – physicians tend to resist changes that upset equilibriums and threaten hegemony over medical procedures and access to patients and funds. Third, the high level of regulation in the medical profession and the stringent safety requirements need to be accommodated.

Regulation

Regulatory approval is an essential step before a medical device can be introduced into a market. Many standards and regulatory bodies exist; each and every country has its own set of rules, regulations and procedures governing the introduction of new medical procedures and pharmaceuticals. The "gold standards" of approvals are those from the US Food and Drug Administration (FDA) and the European Economic Area (EEA), with its CE marking, which has been mandatory for certain products since 1985.

Acquiring regulatory approval for a medical device entails a very clear and uniform roadmap. It requires huge investments of time and money, and the outcomes are uncertain.

Regulatory processes and classifications are extremely elaborate and complex, requiring many years of study (human trials) and experience. For our purposes, a very brief portrayal will do. In

the US, medical devices are classified into three categories (I, II, and III), escalating according to their level of invasiveness and their importance in medical decision making.

Classifications I and II generally require an FDA 510(K) procedure (pronounced five ten kay), which means that the technology is substantially equivalent to an existing one. New technologies are categorized as Class III devices and require a Premarket Application (PMA), which involves several stages of clinical studies and takes much longer.

InSightec sought PMA approval from the outset, mainly in the belief that if one device fails or is discredited for any reason, the rest of the approved devices and indications will remain intact.

Reimbursement

Regulatory approval is an essential stage before a device can be marketed, but it says nothing whatsoever about the economic viability of the product, or the chances of adoption by the medical community.

Reimbursement is the purely economic process of refunding a hospital or medical professional for a medical procedure performed on an insured patient. A medical insurance company will perform reimbursement for a specific procedure only if it saves them money compared to the alternative treatment or if the treatment is significantly better than the existing alternative. Moreover, as economic bodies struggle with ever-increasing costs and very conservative views about adding additional procedures, when faced with an out of the ordinary procedure, insurance companies are inclined to deny reimbursement. Such is the case of essential tremor. Insurance companies never counted on spending anything on treating essential tremor except for the standard medications. As will be demonstrated, a breakthrough treatment exists, and millions of Americans with shaking disorders will demand to undergo the treatment, a treatment on which the insurance companies never planned to spend a single dollar.

It has been shown that without a reliable reimbursement process, some devices will fail because they will have to rely solely on private money. This creates a vicious circle – hospitals or medical professionals that don't expect to get reimbursed will not buy the device in the first place; patients will not become aware of the possibility, and insurance companies will not be compelled to reimburse.

Moreover, the current reality is an extremely stressful one for medical insurance companies as people are living longer and health expenditure is rapidly growing, causing payers to avoid sponsoring new technologies, even if they have the potential to lower payments in the long run.

Company overview

History and ownership (Exhibit 7)

InSightec was established in 1999 by GE Healthcare (then GE Medical Systems) and Elbit Medical Imaging. The company was founded with a clear vision and mission, which still guide it today, to replace surgery with a non-invasive solution, and transform its MR guided focused ultrasound (MRgFUS) into a clinically viable technology

Since its establishment, InSightec has invested close to $250 million in R&D. The company holds over 95 patents with additional intellectual property assets pending approval. It is headquartered in Tirat Carmel, Israel, near the port city of Haifa, and has US offices in Dallas, TX, as well as offices in China, Japan and Europe.

The company made its first attempt to commercialize an application in the field of breast cancer, only to realize that a significant adoption gap exists, since rival alternatives are relatively good. In 2001, it started its first trials to test FUS as a solution for uterine fibroids, a highly pervasive benign gynecological disease. It received CE marking (from the EEA) in 2002 followed by FDA approval (from the US Food & Drug Administration) in 2004, after an extensive series of clinical trials. Since then, the company has received approval from regulatory bodies around the world (including Japan's MHLW, and China's CFDA) to treat uterine fibroids and is in the early stages of worldwide regulatory approval for other indications. It received CE marking for treating bone metastases, its first foray into oncology, in 2007, followed by FDA approval in 2012. Most recently it received CE marking for the treatment of brain disorders and is currently conducting a multicenter clinical trial for FDA approval. InSightec is the first and only company with FDA approval to use MRgFUS for any medical indications.

In 2012, Elbit Medical Imaging sold a portion of InSightec to GE Healthcare under a valuation of $97.4 million, thus losing its control over the company.

It should be noted that GE Healthcare is not only a key investor in InSightec, but also a strategic partner in several areas, including the area of technology (integration of the FUS and MR

systems) and it is a non-exclusive distributor in many countries around the world. As a result, the current FUS systems are only compatible with GE MRI scanners.

Awards

Over the years ExAblate has won several awards for innovation and its potential to help mankind. InSightec has received numerous acknowledgments of its innovative solutions. According to Business Week it produced "one of 25 ideas for a changing world" (2002) and according to Time Magazine "one of 50 best inventions" (2011). In 2008 it was declared a World Economic Forum Pioneer. Among the awards it has received are the European Union IST first prize (2003); the Wall St. Journal's Technology Innovation Prize (2004); and the Red Herring 100 Europe 2007 Award

Organizational structure (Exhibit 8)

The company is divided into two parts: technology, R&D and regulatory issues are the responsibility of InSightec's founder and long-time CEO, Dr. Kobi Vortman; the commercial, marketing and regional functions are the responsibility of the president and CCO, Dr. Robert Sigal. The company employs over 130 engineers, technicians, scientists, sales, marketing and administrative staff.

R&D

As stated, InSightec has spent over $250 million on research and development, spreading itself over numerous treatment indications and geographies. It has also spent considerable sums in seeking regulatory approval in as many geographical locations as possible.

It is important to emphasize the difference between technology R&D (developing the hardware and software that will perform the treatments) and clinical R&D, i.e. generating the clinical data to prove that the system is safe and effective (accomplishes what it is meant to). These clinical data can then be used to achieve regulatory approval, physician acceptance, and reimbursement.

In essence and practicality, InSightec is above all an R&D focused company that has spent more than twice its equity over the years to develop its pioneering technology. InSightec's leadership and culture are steadfastly scientific and technological.

Production

InSightec develops its own devices, manufactures them and offers continuous services to its clients – upgrading hardware and system software. There are two systems under InSightec's ExAblate brand: ExAblate O.R. and ExAblate Neuro. ExAblate units were first introduced in 2002, and since then over 100 have been produced and installed in hospitals and clinics around the globe. All production is carried out at InSightec's HQ facility in Tirat Hcarmel near Haifa. InSightec's products are embedded on GE MRI beds, according to contracts signed between the parties. Other than the MRI beds, which are unique and extremely elaborate systems, the rest of the equipment used is abundantly available, thus nullifying reliance on a specific supplier.

Products (Exhibits 9-11)

Essentially, InSightec has two products for delivering its focused ultrasound systems: ExAblate O.R., designed for treating most areas of the body, and ExAblate Neuro for treating disorders in the head. As of today, InSightec has regulatory approval for treating three medical conditions.

Gynecology

As already stated, InSightec started its business endeavors with an attempt to treat breast cancer with FUS, only to realize that it would take a long time and a very large number of patients to obtain regulatory approval. They therefore looked for a highly prevalent indication that did not have good treatment options, and for which it would not take too long to obtain regulatory approval. Uterine fibroids (UF) fit this bill well and initial treatments began in 2001. Most of InSightec's installed systems are dedicated to treating this indication.

Fibroids are benign tumors that originate in the smooth muscle layer (myometrium) of the uterus and they can seriously impact a woman’s quality of life. Symptoms of UF include heavy

and painful menstruation, painful sexual intercourse, and urinary frequency and urgency. In some cases fibroids may interfere with the ability to conceive.

Up to 25% of women aged 25-50 suffer from symptoms of uterine fibroids and as these symptoms become progressively worse they consider undergoing some medical treatment.

Multiple alternative treatments exist in the UF market. The most prevalent is a hysterectomy, removal of the uterus; the fact that it is also the most invasive and damaging treatment out there also opens up interesting opportunities. The less invasive treatments include myomectomy (surgically extracting the fibroids), and uterine artery embolization (UAE), a minimally invasive treatment that blocks the blood flow to the fibroids, thus depriving them of nourishment and eventually killing them. All these techniques have significant drawbacks, the most noteworthy being the long hospitalization and recovery periods, the painfulness of the procedures, and the fact that they involve a great deal of collateral damage and significantly hinder the chances of conceiving in the future. Moreover, hysterectomy is highly correlated with other medical conditions such as pelvic organ prolapse, urinary and anal incontinence, bowel dysfunction and constipation, as well as Alzheimer's disease, mental illness and cardiovascular diseases.

UF is also the indication for which InSightec has a direct competitor – Philips Medical, which began marketing an MRgFUS system in 2010 with a market share of 40 systems. They obtained CE marking for uterine fibroids on the basis of ExAblate data and are currently undergoing an FDA trial in the US and another one for CFDA approval in China InSightec estimates the UF market at around $3 billion, with approximately 600,000 annual symptom eliminating procedures performed in G7 countries; out of these, 50% are potential candidates to undergo MRgFUS. Grossly, this means around 1,500 potential MRgFUS systems worldwide dedicated to treating only UF.

A study conducted in the UK in 2008 indicates that treating UF with MRgFUS is extremely likely to be significantly cost effective compared to surgical procedures. It is estimated that it will directly save almost £300 per procedure, and has better results compared to the more traditional techniques. Furthermore, taking into account the extensive recovery time patients undergoing hysterectomy experience (4-6 weeks of complete bed rest), MRgFUS would save more than £500 per patient. A recent paper published in the US shows that despite the

impression that image guidance and the high cost of MRI makes MRgFUS more expensive than other treatments for UF, the two-year costs (one year before treatment and one year after) are of the same order of magnitude: MRgFUS – $19,762; myomectomy – $20,407; and UAE – $25,019 (Borah et al. Cost comparison between uterine-sparing fibroid treatments one year following treatment. Journal of Therapeutic Ultrasound 2014, 2:7).

These findings entirely disregard the reproductive implications of alternative treatments. When taking these into account, the benefits to women of childbearing age are simply inestimable. Recent studies have shown that fertile women who underwent FUS to treat UF were able not only to conceive, but also gave birth naturally and without complications.

As discussed earlier in the case, FUS has the power to revolutionize the medical profession in terms of ownership of treatments and procedures. Traditionally, in the case of UF gynecologists were the designated professionals to treat women suffering from this condition. Moreover, specialists in obstetrics and gynecology (OBGYNs) were also the primary caregivers and possessed the holistic knowledge of how to treat this and other gynecological ailments. However, once FUS was introduced, interventional radiologists began performing the non-invasive procedures. With their advanced knowledge and proficiency in operating the MRI beds, they are indeed ideal candidates to perform the diagnosis as well as the interventional procedure. This shift caused OBGYNs to abstain from pursuing the alternative non-invasive procedure, and even to hinder efforts to adopt it in the medical facility in which they operate.

Bone

As cancers advance they spread to other parts of the body, and one of the most common sites to which these secondary cancers, known as metastases, spread is to the body's bone tissue. Most patients with bone metastases suffer from crippling pain, further hampering their ability to cope with the cancer itself.

Luckily, bone tissue is a perfect absorbent of ultrasound waves, making it an optimal target site for FUS treatments. Since InSightec performed its first bone treatment in 2005, hundreds of cancer patients have been through this palliative procedure, enabling them to continue living a relatively normal life, despite their malignant cancer. Since the development of the Bone I apparatus, InSightec has developed its conformal bone system (CBS), which is able to more

easily and conveniently access treatment locations. The transducers are hand-held, and the patients are positioned comfortably during the treatment's duration (to date, the CBS has received only CE marking, while Bone I has both CE marking and FDA approval).

The results of MRgFUS on bone metastases are astounding. Patients have testified that three days after the treatment, almost all pain symptoms were alleviated, and most have attested to significant pain reduction from day one. The procedure itself is extremely painful, however, and requires local sedation, or in some cases even general anesthesia.

A handful of treatments for bone metastases exist in the market. Most are effective, and each has its drawbacks and advantages.

The classic treatment for this condition is radiation, despite its harmful side effects. Generally, patients who do not respond well to radiation are referred to the numerous alternative treatments in the field.

Radiofrequency ablation (RFA) and microwave ablation are treatments that ultimately have the same effect on the corrupt tissue as FUS, but do so in a more invasive manner and are not as effective. Another treatment is cryoablation, which applies the same principle, but uses extreme cold to kill the tissue instead of heat. FUS is considered safer, causing less skin burns than alternative treatments, and no neurologic repercussions or infections, since it is totally non-invasive and highly focused.

The global bone metastases market is estimated to be around $10 billion, treating approximately 920,000 patients, of whom 50% are eligible for MRgFUS treatment. This means a potential for roughly 2,000 systems worldwide dedicated only to the treatment of this condition. In the case of bone metastases the question of process ownership is also important. The patient is seen initially by a medical oncologist (or an organ specialist such as a pneumologist or gastroenterologist). For bone metastases, the referral today is irradiation performed by radiation oncologists, not radiologists. Referrals are rarely made to Interventional radiologists and then only in a limited number of situations where there is a risk of bone fracture or when alternative treatments such as RFA or cryoablation are sought.

<u>Brain</u>

The brain and central nervous system have always been the main and most fascinating frontier for focused ultrasound treatments, and they were the area first investigated by the pioneers of FUS in the 1940s and 1950s. Since its inception InSightec has been working to overcome the significant challenges of non-invasive treatment of the brain.

In 2012 InSightec received its first CE marking for treatment through an intact skull for movement disorders such as essential tremor and certain forms of Parkinson's disease (tremor dominant), a disorder affecting more than 10 million people in the US alone. Once believed to be old age disorders, nowadays both essential tremor and Parkinson's manifest themselves in younger adults too, and are prevalent in all segments of society.

As symptoms progress, patients are put on an increasing regimen of drugs and then drug cocktails that help alleviate symptoms. Patients who have exhausted the pharmaceutical options have one major alternative treatment to consider – deep brain stimulation (DBS), which involves inserting electrodes into the relevant brain site and sending electrical stimuli to regulate neurological discharge. The electrodes are connected to a power source implanted in the patient's chest. Inserting the device requires a full surgical procedure with all its consequences and hazards. MRgFUS offers a totally non-invasive option, performed while the patient is fully awake, providing feedback as to any discomfort or sensations during the procedure.

Remarkable outcomes have been documented. People who have been shaking for years and been completely dependent on caregivers to accomplish basic day to day actions get up after the procedure and simply take a confident sip of water or write a coherent thank you note. These are trivial things for most of the population, but astounding feats for those with a chronic tremor.

The neurological movement market is estimated to be around $26 billion globally, with 100,000 new functional-neuro patients annually. All are considered as viable candidates for MRgFUS, leading to an estimation of 800 potential systems.

The next steps for neurological solutions for FUS are treating epilepsy, brain tumors, and psychiatric conditions such as OCD and depression. Each year 400,000 people are diagnosed with brain tumors; it is estimated that 50% will be treatable using MRgFUS.

Treating the brain with this or any other system for that matter is truly the most ambitious of medical interventions. Relying on current data, the neurological arena holds immense potential yet untapped.

InSightec's regulatory status (Exhibit 12)

Since InSightec was the first in the market, it received FDA approval and CE marking more rapidly than the competitors that followed. Regulatory approval allows the company to legally label and market the device throughout the relevant geographies (in the US for FDA approval, in the European Union countries for CE marking, etc.), but once approval is received from both these bodies, the rest of the world usually follows. The specific labeling however places strict limitations on what you can or cannot write on the marketing leaflet. For example, the approval granted for ExAblate O.R. to treat UF does not allow InSightec to mention that the treatment will help treated women to get pregnant again. This is despite the fact that research has certainly shown that it does, as opposed to alternative treatments.

Furthermore, receiving regulatory approval is harder for some indications than for others. For example, receiving CE marking for ExAblate Neuro to treat shaking disorders was significantly easier than for any other indication due to the fact that following the treatment patients immediately ceased to shake, an extremely strong indication of the treatment's effectiveness. Of course you need to prove that the procedure is also safe, which requires longer tests and observations, but this became apparent very quickly too. By contrast, approving ExAblate MRgFUS as a treatment for breast cancer may require years of clinical trials to prove its efficacy and safety. The full cycle to get regulatory approval may take between three and six years.

ExAblate O.R. received its first European CE marking in 2002 and FDA approval in 2004 for the treatment of symptomatic uterine fibroids. In June 2007, it received CE marking for pain palliation of bone tumors and, in June 2010, for adenomyosis. In 2012, ExAblate O.R. received its second FDA approval for pain palliation of bone metastases and ExAblate Neuro received CE marking for the treatment of neurological disorders such as essential tremor, Parkinson's and neuropathic pain. In 2013, CE marking was extended to other painful bone indications including primary and secondary bone cancers as well as benign diseases such as facet joint pain and osteoid osteoma

Reimbursement

Some of InSightec's procedures do receive reimbursement, depending on geographies, but not enough to allow effective market penetration and proliferation of devices. For example, the treatment of uterine fibroids is still not reimbursed in the US.

Current business model

Marketing

InSightec invests a modest portion of its budget on marketing and sales promotion; in 2013, the budget for global marketing was approximately 3% of global sales. Marketing efforts rely mainly on peer reviewed research by leading physicians, published in medical journals as well as talks given at conferences. Marketing is aimed at raising awareness among the relevant physicians, that is, gynecologists and radiologists for uterine fibroids and radiation oncologists and interventional oncologists for oncology indications. It includes stands at professional medical conferences, mainly those of radiologists, both diagnostic and interventional. Roughly, 40% of marketing expenditure is on conferences and events, with an additional 40% on web presence, and the rest on miscellaneous efforts.

Sales & distribution (Exhibits 13-16)

Globally, InSightec is represented by distributors in charge of a certain region. Since it has GE Healthcare on its side, many distributors are GE owned, but others work for InSightec. InSightec has established clinical collaborations with leading hospitals and medical research institutions around the world, many of which participate in sponsored trials to gather clinical data that will advance the company’s technology and create an ever-widening spectrum of clinical applications.

InSightec has over 100 systems installed globally, some of which are not in use for reimbursement reasons, lack of proficient personnel, and lack of awareness of their potential. The largest number of MRgFUS systems is in the US, but they can also be found in Kazakhstan and Vietnam, perhaps the least probable locations for these state of the art solutions.

The Russian market is the busiest and most profitable globally, followed by the very brisk German market, thanks to a single clinic where a physician performs regular UF treatments. InSightec performs most of its initial trials In Israel, and maintains very close contacts with health institutions and professionals in order to develop and improve devices and procedures.

Value proposition

InSightec is continuously making efforts and investing funds to develop new treatments for additional indications where MRgFUS is expected to be effective. As of today, the three indications that have already received regulatory approval are non-life threatening ailments. But if cancer can be cured applying a non-invasive procedure, now that would be an unprecedented feat.

The treatments provided by InSightec's equipment, both approved and potential, hold the promise to change the way interventional medicine is practiced. The following and other factors make this revolution possible:

- Incisionless (non-invasive) procedures without anesthesia
- Outpatient procedure (2-4 hours)
- Short recovery, low trauma & morbidity
- Patient returns to normal activity on the next day
- Minimal complications (infections, adverse surgical events, transfusions, etc.)
- No long-term toxicity or dose accumulation – repeatable procedure
- Green surgery – no sterilization or bio-hazardous waste

Currently, InSightec is conducting clinical trials aimed at receiving approval to treat liver, prostate, and breast cancers. Following the success of treating essential tremor using ExAblate Neuro, approval is also being sought for devices that use the same principle to treat other neurological movement disorders.

The Main Dilemma (Exhibits 17-20)

With its R&D excellence, the cutting edge technologies that InSightec has introduced into the market since its inception have brought it global acknowledgment, market leadership, and further investments. Nevertheless, the company has yet to achieve the commercial success it

deserves. To do so, it needs to develop an effective business model to create sustainable competitive advantage and generate high revenues and profitability.

Management has set a goal to independently achieve sales of $125 million in 2018 with its three current lines of applications (women's health, oncology, and neuro). It intends to keep its headquarters and R&D in Israel and the current shareholders do not intend to sell the company.

Attaining its ambitious objective will require tackling numerous strategic questions, including the following:

- **Market awareness:**
  - How does InSightec raise awareness and commitment among the three main stakeholders: patients (women with uterine fibroids, patients with bone metastases, etc.); physicians who "own" the patients, but not necessarily the technology; and payers/government (public healthcare agencies, medical insurance companies, ministry of health officials, elected member of government)
  - Is there one particular stakeholder that could drive the change?
  - Would rebranding the product to a more memorable name bring about this change?
- **Business model:**

  In 2013 InSightec spent 58% of its resources on R&D and 37% on sales and marketing. Is this a sustainable model to reach the financial objectives?

- **Markets:**

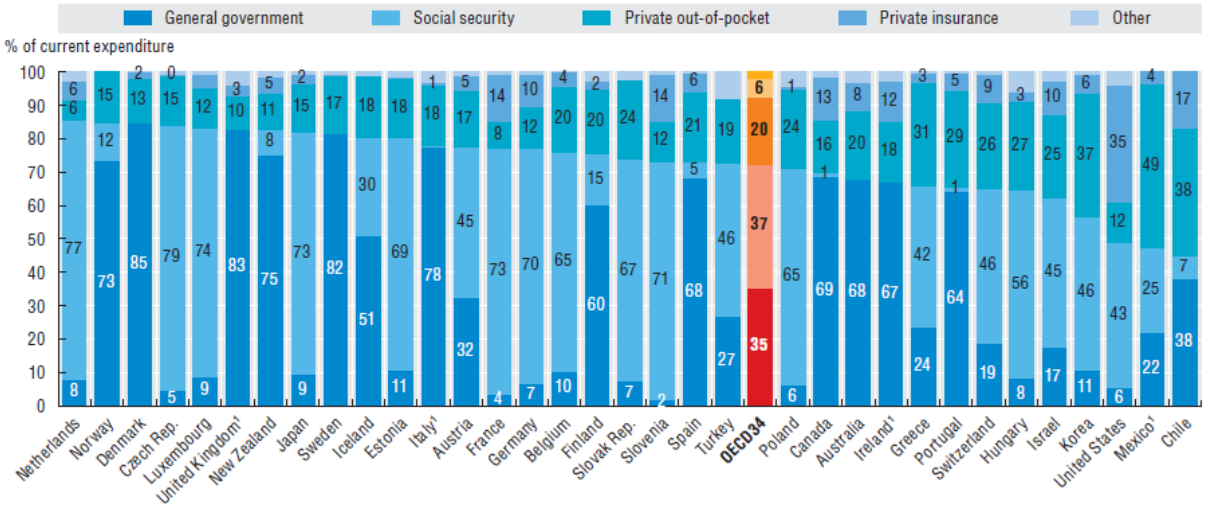
  Today, InSightec actively sells in over 15 countries in the Americas, Asia and Europe. Should it concentrate activities or expand?

In addressing these questions the company should take into account issues such as marketing and distribution channels, sales force, and developing a strong market brand.

Tackling a new business model will require InSightec to reallocate its resources and capabilities, installing mechanisms that will enable it to "cross the chasm" on the roadmap to prosperity and accomplishment.

Appendixes

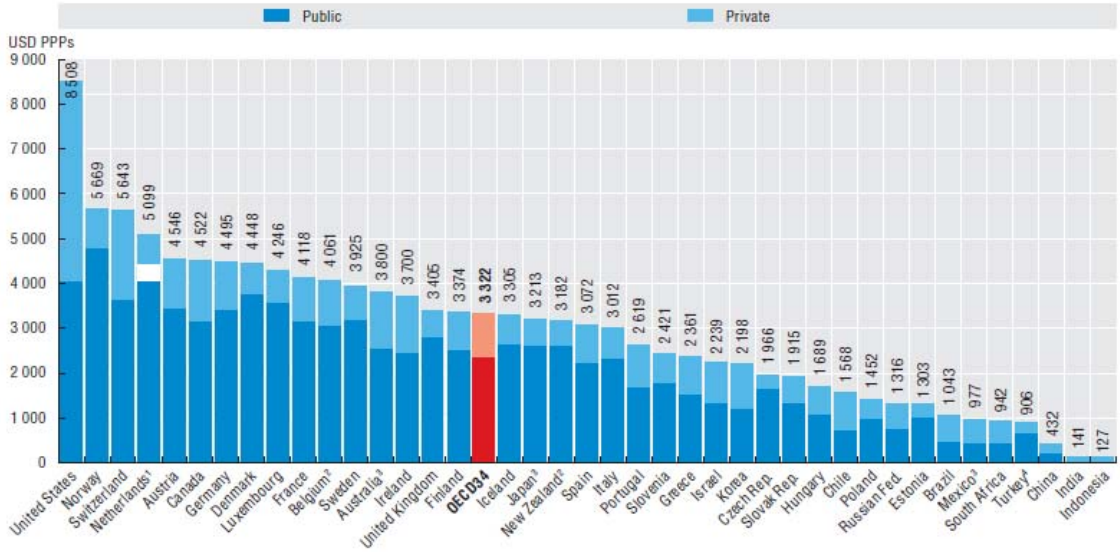
Exhibit 1: Healthcare expenditure by type of financing, OECD countries, 2011



1. Data refer to total health expenditure.

Source: OECD Health Statistics 2013, http://dx.doi.org/10.1787/health-data-en.

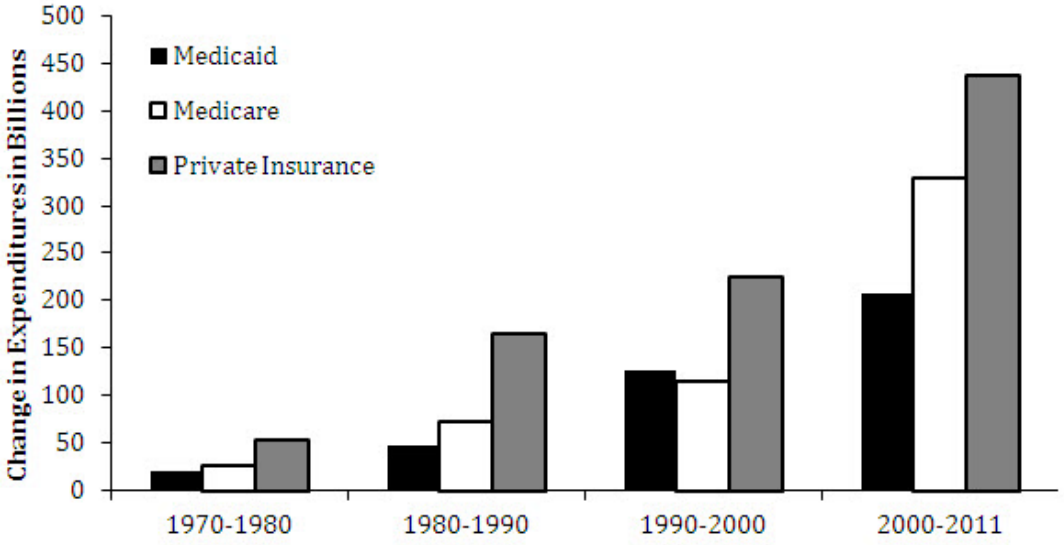
Exhibit 2: Healthcare expenditure per capita, 2011



1. In the Netherlands, it is not possible to clearly distinguish the public and private share related to investments.
2. Current health expenditure.
3. Data refer to 2010.
4. Data refer to 2008.

Source: OECD Health Statistics 2013, http://dx.doi.org/10.1787/health-data-en; WHO Global Health Expenditure Database.

Exhibit 3: Change in overall national healthcare expenditure in the US, 1970–2011, $US billion



Source: Centers for Medicare & Medicaid Services, Office of the Actuary, National Health Statistics Group, Historic National Health Expenditure Data.

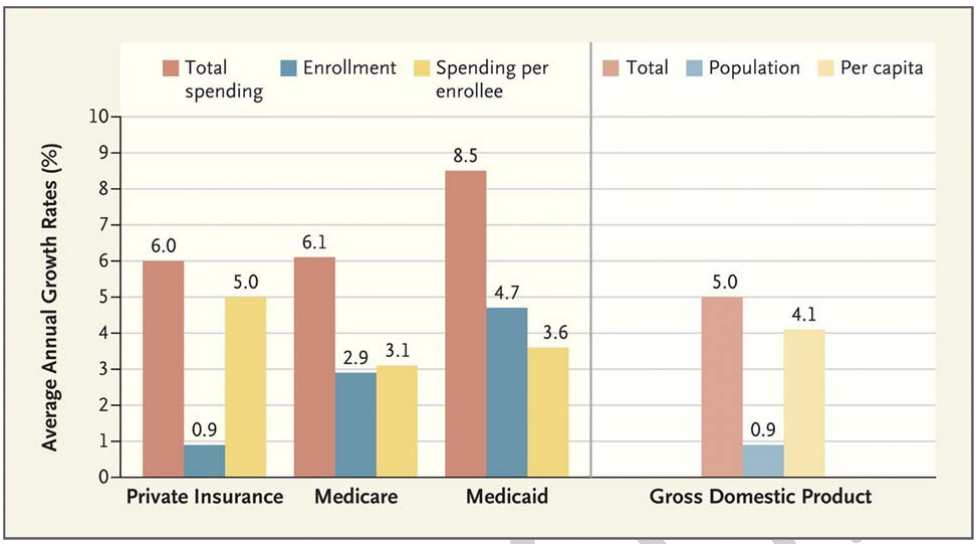
Exhibit 4: Private sector spending across the continuum of care in the US

Care Domain	2001	2003	2005	2007	2009	2011
	Amount in Billions of Dollars					
Physician and Clinical Services	70.2	81.0	95.0	107.0	131.5	139.9
Hospital Care	135.0	150.9	176.4	193.8	216.4	231.3
Post-Acute Care and Other	25.2	31.7	42.2	53.1	64.8	75.6
Pharmaceutical	2.4	2.5	3.9	46.0	54.6	63.7
Durable Medical Equipment	4.5	6.0	6.4	7.0	7.5	7.7
Other Non-Durable Medical Equipment	1.6	1.9	2.1	2.5	2.8	3.2

*Figures do not include administrative costs or the net cost of health insurance

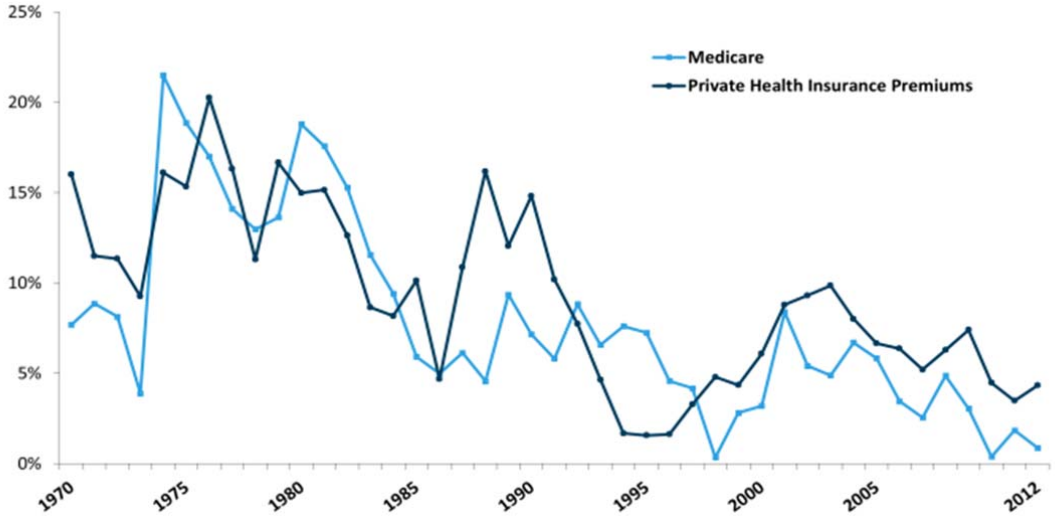
Source: Centers for Medicare & Medicaid Services, Office of the Actuary, National Health Statistics Group, Historic National Health Expenditure Data.

Exhibit 5: Average annual growth rate per enrollee in the US, 2012–2021



Source: Holahan and McMorrow, New England Journal of Medicine, August 2, 2012

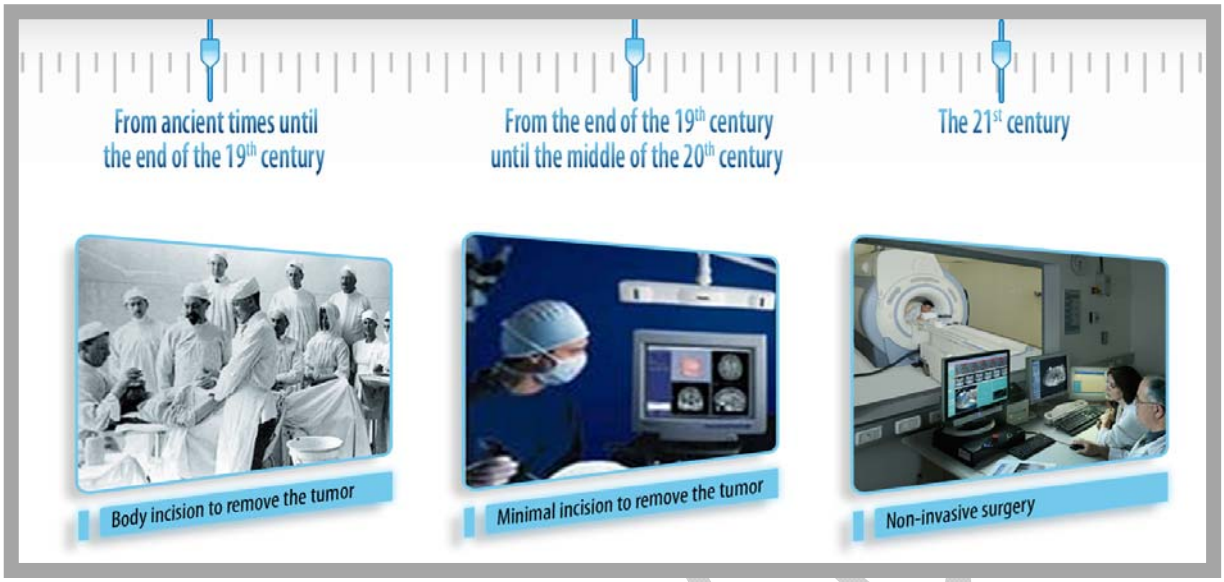
Exhibit 6: Per enrollee growth in Medicare spending and private health insurance premiums (for common benefits) in the US, 1970–2012



NOTE: Per enrollee includes primary policy-holder plus dependents. Common benefits include hospital services, physician and clinical services, ot professional services, and durable medical products; they exclude, for example, prescription drugs, home health care, non-durable medical products, and nursing home care.

SOURCE: Kaiser Family Foundation calculations using NHE data from Centers for Medicare and Medicaid Services, Office of the Actuary, National Health Statistics Group, at http://www.cms.hhs.gov/NationalHealthExpendData/ (see Historical; NHE Web tables, Table 21).

Exhibit 7: InSightec's vision of the evolving of surgery



Source: company data

Exhibit 8: InSightec – no. of employees by sector, 2013

	Total	%
Manufacturing	25	19
Sales and marketing	20	15
R&D	67	52
Corporate	14	11
Additional senior staff	4	3
Total	130	100

Source: company data

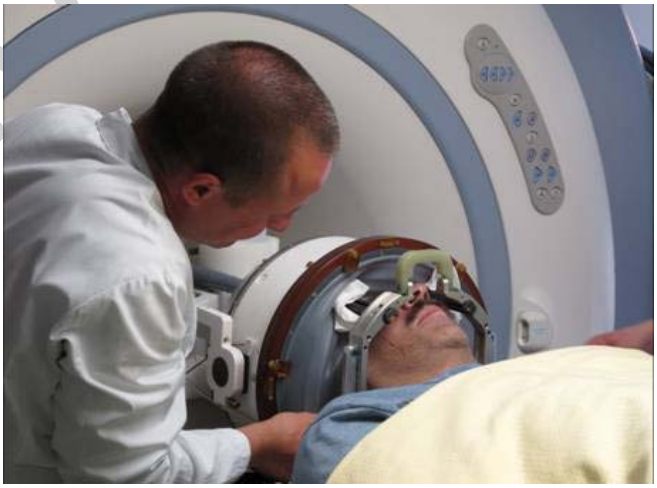
Exhibit 9: InSightec – MR guided focused ultrasound – a combination of two technologies

High intensity focused ultrasound
to heat and destroy targeted tissue

Magnetic resonance imaging (MRI)
for precise visualization, guidance and real time control

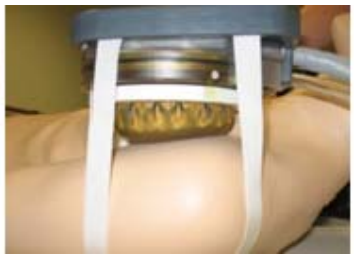
&

Exhibit 10: MR guided FUS, a developing neurosurgical subspecialty

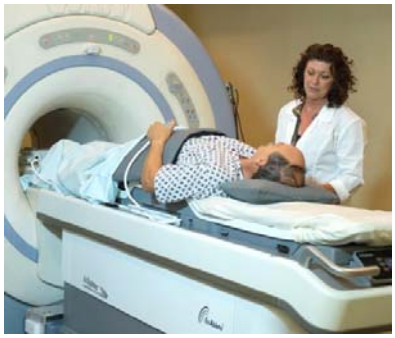


The brain unit

Exhibit 11: MR guided bone and body unit



The bone unit



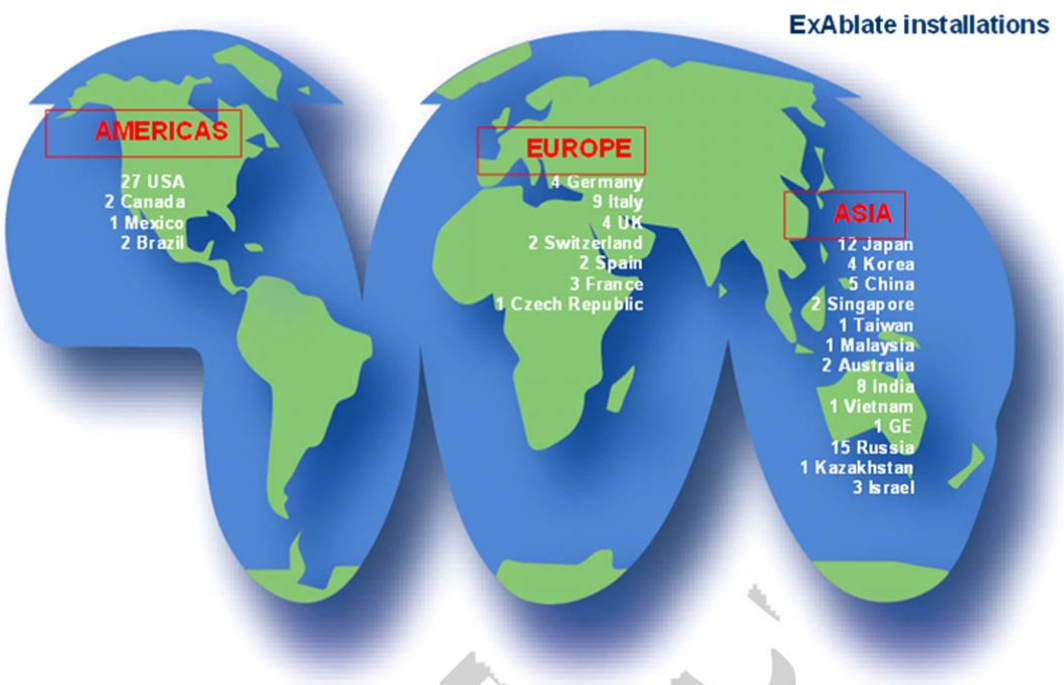
The body unit

Exhibit 12: InSightec's regulatory status

Application	FDA (USA)	CE Marking (Europe)	MHLW (Japan)	KFDA (Korea)	CFDA (China)
Uterine Fibroids	o	o	o	o	o
	2004	2002	2009	2005	2013
Adenomyosis	-	o		o	
		2010		2011	
Bone Metastasis (Bone1)	o	o	-	o	
	2012	2007		2009	
Bone Metastasis (CBS)	IDE Phase 2	o	-	o	
Primary/secondary bone tumors: benign and cancerous		o			
		2013			
Multiple myeloma	-	o	-		
		2013			
Facet rhizotomy	-	o	-	-	
		2013			
Breast cancer	-	-	-	o	
				2005	
Prostate cancer	Phase 1	-	-	-	
Essential tremors / PD tremor dominant	Phase 3 Phase 1	o	-	o	
Neuropathic pain		2012		2011 (under KFDA - only research)	

Source: company data

Exhibit 13: InSightec's global installations, 2013



Source: company data

Exhibit 14: InSightec's sales – geographical breakdown

	2011	2012	2013
America	26%	28%	14%
Europe	32%	40%	49%
RoW	42%	32%	37%
Total	100%	100%	100%

Source: company data

Exhibit 15: Main competitors

Philips Healthcare

Royal Philips, commonly known as Philips, is a Dutch diversified technology company headquartered in Amsterdam. One of the largest electronics companies in the world, employing around 122,000 people across more than 60 countries, Philips is organized into three main divisions: Philips Consumer Lifestyle (formerly Philips Consumer Electronics and Philips Domestic

Appliances and Personal Care), Philips Healthcare (formerly Philips Medical Systems) and Philips Lighting.

They began offering Sonalleve, using MRgHIFU (their version of MRgFUS) in 2010, obtaining CE marking for uterine fibroids and bone metastases. They are currently running a clinical trial for FDA approval in the US and CFDA approval in China for uterine fibroids and some initial bone metastases trials.

Philips is considered by some in the market as less advanced than its competitors from a clinical standpoint. Moreover, they do not offer a neuro line of products.

EDAP TMS

EDAP TMS S.A. founded in 1979 and based in Vaulx-en-Velin, France, engages in the development, production, marketing, distribution, and maintenance of minimally invasive medical devices for the treatment of urological diseases. The company operates in two divisions: High Intensity Focused Ultrasound (HIFU), and Urology Devices and Services (UDS). The HIFU division offers medical devices for the minimally invasive destruction of various types of localized tumors using HIFU technology. This division provides Ablatherm, a HIFU-based ultrasound guided device for the treatment of organ-confined prostate cancer.

FUS Instruments

FUS Instruments is a privately owned company from Toronto, Canada, that spun out of the Sunnybrook Research Institute at the University of Toronto in 2009.

FUS Instruments develops image-guided focused ultrasound systems for preclinical research. The technology line includes systems that are compatible with large and small bore MRI and CT systems, and diagnostic ultrasound.

Sonacare Medical

SonaCare Medical, a privately held, venture-backed healthcare company founded in 2004 and headquartered in Charlotte, North Carolina, claims to be a world leader in minimally invasive high intensity focused ultrasound (HIFU) technologies. SonaCare Medical, with its subsidiary Focus Surgery, Inc., designs and manufactures high intensity focused ultrasound (HIFU) medical devices, including the following: Sonablate® 450, which is investigational in the US and is being

studied in a pivotal FDA clinical trial as a possible treatment for recurrent prostate cancer in patients treated previously with external beam radiation therapy; Sonablate® 500, which has CE marking and is, or has been, approved for use to treat prostate cancer in more than 30 countries outside the US; and the Sonatherm® laparoscopic HIFU surgical ablation system.

Exhibit 16: Competitive solutions in the market

EDAP TMS / Ablatherm HIFU

Ablatherm® HIFU is a robotic HIFU device (High Intensity Focused Ultrasound) for the treatment of localized prostate cancer. Using a non-invasive transrectal approach, it can be used for partial or whole-gland ablation as a first-line or as a salvage therapy for recurrence after radiotherapy. The integrated imaging transducer allows precise planning of the area to be ablated and real-time visual control during the treatment.

EDAP TMS / Focal One

Focal One® is the first device dedicated to the focal approach of prostate cancer therapy by combining the three essential components to efficiently perform a focal treatment: (i) state-of-the-art imaging to localize tumors with the use of MRI combined with real-time ultrasound (elastic fusion), (ii) utmost precision of robotic HIFU treatment focused on identified targeted cancer areas only (Dynamic Focusing technology) and (iii) immediate feedback on treatment efficacy with Contrast-Enhanced Ultrasound Imaging.

FUS Instruments / RK100

The RK100 is a versatile preclinical focused ultrasound system designed to function as a platform for focused ultrasound research. The system utilizes real-time MR or CT guidance to deliver precise exposures to small structures in both small and moderate sized animal models. The RK100 can operate inside of a full-size MRI bore and can produce ultrasonic exposures up to 100 W.

FUS Instruments / RK300

The RK300 is a focused ultrasound system manufactured to be used within small-bore preclinical imaging systems. This platform is specifically designed for the exposure of small animal models and is particularly suited for blood-brain barrier opening studies. It includes image-guided targeting software, an integrated computer controlled high precision two-axis positioning system and a calibrated focused ultrasound transducer.

InSightec / ExAblate

InSightec Ltd is the pioneer and global leader in MR guided focused ultrasound technology. Founded in 1999 and owned by Elbit Imaging and GE Healthcare, its product ExAblate, using MR guided Focused Ultrasound (MRgFUS) technology, is the operating room of the future. InSightec holds over 90 patents with additional intellectual property pending. It is headquartered in Tirat Carmel, Israel, with offices in Dallas, TX, Europe and Asia.

ExAblate for the treatment of bone metastases

ExAblate for the treatment of uterine fibroids

ExAblate Neuro for the treatment of functional brain disorders

Mettler Electronics / Sonicator 740

The Sonicator® 740 portable therapeutic ultrasound features a display that is visible regardless of ambient room lighting. Soft controls provide one-touch entry for treatment parameters. The Sonicator 740 has a dual-frequency 5 cm² applicator. 10 cm² and 1 cm² applicators are also available. All applicators feature special coatings that allow direct crystal-to-patient contact. The larger applicators have blue LEDs that indicate adequate coupling.

Source: Company data

Exhibit 17: InSightec's consolidated statement of income, in thousands of $US

	31/12/2010	31/12/2011	31/12/2012	31/12/2013
Revenues	**9,001**	**14,704**	**18,002**	**20,672**
Cost of revenues	(6,569)	(8,486)	(9,160)	(9,590)
Gross profit	**2,432**	**6,218**	**8,842**	**11,082**
	27.0%	42.3%	49.1%	53.6%
Operating expenses				
Research and development, net of participation of $1,294, $1,102, 1,381 and 2,781, at 31 December 2013, 2012, 2011, 2010, respectively	(15,108)	(16,376)	(10,811)	(12,074)
Sales and marketing expenses	(6,561)	(5,715)	(5,198)	(7,590)
General and administrative	(4,169)	(13,334)	(3,718)	(4,322)
Operating profit (loss)	**(23,406)**	**(29,207)**	**(10,885)**	**(12,904)**
Financial income	(1,997)	258	(2,337)	(93)
Profit (loss) before taxes on income	**(25,403)**	**(28,949)**	**(13,222)**	**(12,997)**
Taxes on income	(140)	(208)	(60)	(10)
Net profit (loss)	**(25,543)**	**(29,157)**	**(13,282)**	**(13,007)**

Exhibit 18: InSightec's balance sheets, in thousands of $US

	31/12/2011	31/12/2012	31/12/2013
Current assets			
Cash and cash equivalents	1,228	21,838	1,796
Restricted cash	48		
Deposits			5,004
Receivables			
Trade accounts receivables, net of allowance for doubtful accounts of $0, $43 and $43 at December 31, 2013, 2o12 and 2011	1,631	1,923	4,221
Inventories	1,969	2,849	3,664
Other receivables and current assets	716	2,109	1,250
Total current assets	**5,592**	**28,719**	**15,935**
Fixed assets, net	697	384	311
Prepaid expenses and restricted cash	**304**	**135**	111
Total assets	**6,593**	**29,238**	**16,357**
Liabilities and shareholders' equity (deficiency)			
Current liabilities			
Trade accounts payable	2,307	2,967	3,174
Other payable and current liabilities	19,615	9,769	**8,836**
	21,922	**12,736**	**12,010**
Long-term liabilities			
Long-term loans from related parties and other	33,985	1,305	1,013
Shareholders' equity (deficiency)			
Ordinary shares	35	35	35
Preferred shares	34	192	**192**
Additional paid-in capital	155,397	233,033	234,177
Cumulative deficit	(204,780)	(218,062)	(231,069)
	(49,314)	15,197	3,334
Total Liabilities	**6,593**	**29,238**	**16,357**

Exhibit 19: InSightec's expenditure by sector, 2010–2013

	$, thousands				% of annual revenues			
Year	**2010**	**2011**	**2012**	**2013**	**2010**	**2011**	**2012**	**2013**
Revenues	9,001	14,704	18,002	20,672				
Sales and marketing	6,561	5,715	5,198	7,590	73%	39%	29%	37%
R&D	15,108	16,376	10,811	12,074	168%	111%	60%	58%
General and admin	4,169	13,334	3,718	4,322	46%	91%	21%	21%

Source: company data

Exhibit 20: InSightec's inventory, in thousands of $US

Year	**2011**	**2012**	**2013**
Raw materials	1,909	2,656	2,895
Finished goods	60	193	769
Total	1,969	2,849	3,798

Source: company data