Horizon Scanning report N°3

Minimally invasive treatment for atrial fibrillation by high intensity ultrasound (HIFU) ablation

July 2009

Methods:

Agenas is a public body. Its mission is to promote innovations and developments within the Italian national healthcare service and develop a Horizon Scanning (HS) function within healthcare technologies.

A full description of the methods used and the process phases undertaken for HS, can be found at www.agenas.it.

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Limitations:

This report is based on information available when the searches were made and does not contain data on subsequent developments or improvements of the evaluated technology. The observations made on effectiveness, safety or cost-effectiveness of the technology evaluated in the report are to be considered temporary.

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Name of the technology/procedure: **Minimally invasive treatment for atrial fibrillation by high frequency ultrasound (HIFU) ablation**

Target population

The technology is aimed at patients who suffer from atrial fibrillation (AF) and who have shown resistance to other pharmacological therapies and/or have received treatment by transcatheter ablation which was ineffective.

Description of the procedure and technology

Ablation consists of causing lesions on heart tissue to electrically isolate certain areas and restore normal heart impulse conduction. The lesions are normally made in specific segments (for example; around the pulmonary veins), using different sources of energy and different approaches (endocardiac or epicadiac) [Aktas, 2008]. The procedure of high intensity focused ultrasound (HIFU) ablation can be performed in open chest procedure, or by means of a small incision between the ribs (mini-thoracotomy). In the second instance the procedure is defined as minimally invasive. The present HS report assess those devices which by means of ultrasound are capable of inducing localised lesions following a minimally invasive approach.

Clinical importance and burden of disease

AF is a cardiac arrhythmia characterised by irregular electrical activity of the atria, two of the four heart chambers. Normal atrial contractions are replaced by chaotic movements which are not effective in achieving blood propulsion. According to prevalence estimates, some 2.3 million Americans have AF, although this figure seems to be destined to double by 2050 because of different causes, amongst them the ageing of the population [Kannel, 2009].

AF is the most common cardiac arrhythmia in clinical practice and its incidence is age-dependent [Disertori, 2006]. One estimate puts its prevalence in Europe at 4.5 million cases [Fuster, 2006], while in Italy it is estimated that there are 400,000 sufferers and 50,000 new cases every year [Disertori, 2006]. AF is more common in Caucasians than Africans [Ruo 2004].

There has been a 66% increase in hospitalization for AF in the last 20 years. This is due to the ageing population and to the increase in chronic cardiac diseases and an increased diagnostic capability in outpatients [Fuster, 2006].

AF is associated with sizeable increase in morbidity and mortality especially in asymptomatic patients. Risks of stroke, cardiac failure and cardiomiopathy caused by tachycardia are all increased by AF. In the US 15-20% of strokes may be associated with AF [Hart, 2000].

Patients with symptomatic AF have a lower quality of life with palpitations, chest pain, dyspnoea, fatigue and hypotension as main symptoms. On the basis of severity, several types of AF can be described as follows:

- paroxysmal: a patient with episodes lasting up to 7 days with spontaneous conversion to sinus rhythm;
- persistent: a patient with episodes lasting longer than 7 with conversion to sinus rhythm after pharmacological or electrical cardioversion;
- permanent: a patient with permanent AF.

AF presents itself with co-morbidities (such as hypertensive cardiopathy, ischaemic cardiopathy, cardiac failure, cardiomyopathies, mitral valve disease). However it can present itself in the absence of co-morbidities (isolated or idiopathic AF) in an estimated 15 to 30% of cases [www.fibrillazioneatriale.it]. In addition an estimated 50% of patients with mitral valve disease have associated AF. After heart surgery, 15-20% of cases convert into sinus rhythm without any specific anti-arrhythmic treatment [www.fibrillazioneatriale.it].

Manufacturers, distributors and approval

At the time of writing (July 2009) we could identify only one manufacturer of minimally invasive HIFU ablation technology: St Jude Medical Inc. In Italy, the company also distributes the kit. The kit includes a circular ablation device called UltraCinch, a straight ablation device called UltraWand, the introducer, a link cable and the ablation control system. The system is called Epicor LP and is an evolution of Epicor which has been on the market since 2006 and is used only for open chest surgery [www.sjm.com/].

The Epicor LP system was approved by the FDA in September 2008 and received the CE mark in November 2008. The relevant documentation is present in the Inventory of Medical Devices (RDM) of the Italian Ministry of Labour, Health and Social Policies (MLSPS).

According to the manufacturer' instructions the system must be used *"for tissue ablation during cardiac surgery and has been designed specifically for epicardial application on a pulsating heart"*.

We are aware that other companies are developing minimally invasive cardiac ablation systems: Atrionix; Atritech; Cryocath Technologies, CardioFocus; ProRhythm; Toray Industries, Hansen Medical [Reddy, 2009]. Among these only Atrionix and ProRhythm are developing HIFU-based systems [Schmidt, 2007].

Manufacturers	Distributors	CE Mark	RDM	FDA
St. Jude Medical Inc.	St. Jude Medical Inc.	☑	☑	☑

Key: RDM = Repertorio nazionale Dispositivi Medici (Italian medical devices inventory); FDA = US Food and Drug Administration

Setting

The procedure is carried out in hospital, in the cardiac surgery theatre or in the hybrid theatre (a sterile theatre with the equipment for the procedure).

☐ Home	☑ Hospital	☐ Out patients
☐ Accident and Emergency	☐ Other:	

Roll out in Italy

The Epicor LP system has been on the Italian market since November 2008. At present the manufacturer reports only one centre active in mini-thoracotomy procedures, at the Luigi Sacco Hospital in Milan (10 cases had been operated on by June 2009).

☐ Pre-marketing	☐ On the market for 1-6 months	☑ On the market for 7-12 months
☐ On the market for more than 12 months	☐ Not identified	

Comparators

At present possible comparators are:

- Open chest surgery;
- Pharmacological treatment;
- Electrical cardioversion;
- Catheter ablation.

Effectiveness and safety

We carried out a review of the literature to identify *Horizon Scanning (HS)* and *rapid Health Technology Assessment (HTA)* reports on minimally invasive ultrasound ablation. We only searched for English language documents in two databases CRD (Dare and HTA) and Euroscan. No reports were identified. The only other report [CEDIT, 2006] assessed the use of an ultrasound ablation system during open chest surgery (the device was Epicor by St.Jude Medical Inc).

We carried out a review of the literature to identify single studies assessing minimally invasive ultrasound ablation using the main search engines EMBASE, Medline and Cochrane Library. We looked for studies in English published in the last 10 years but found none. As it is an emerging technology we also looked for evidence in grey literature (registers, abstracts and presentations). We found no studies or evidence. We are aware that a report of the experience gained with the 10 cases is currently being written.

Potential benefits to patients

The treatment of AF with the Epicor LP system using a mini thoracotomy aims at re-establishing sinus rhythm and cardiac frequency, minimize the risk of blood clots forming and the risk of stroke while intervening on the patient with minimal invasivity. In addition the use of HIFU allows intervention without cardiac arrest and is highly reproducible as the nature of the lesions caused by ablation is less operator-dependent than of those caused using previous devices. If the methods have equal effectiveness the risk of operator dependent failure is less (i.e., due to less dexterity, experience or concentration).

☐ Mortality reduction or increased survival	☑ Reduction of the morbidity	☑ Improved quality of life (patient/user)
☐ Improved patient monitoring	☐ Other:	☐ Not identified

Cost of the technology/procedure

The price of the Epicor LP system recommended by St Jude Medical Inc. is based on the number of procedures carried out (approximately € 2.000-2.500 per procedure). The cost of each Epicor LP procedure borne by the user (health authority or hospital) is based on:

- The Epicor LP system made up of disposable items (circular ablation device, straight line ablation device, introducer and link cable) and by the ablation control system (usually provided in service);
- Staff costs.

The NHS reimburses surgical ablation procedures with the DRG 108 tariff (other cardiovascular system interventions) which is € 12.498,25 per admission; if the procedure is concomitant with another only the principal procedure is reimbursed. This could be a negative incentive for the use of the procedure (and the technology).

☐ Increased costs compared to alternative treatments	☑ Increased costs due to increased demand	☐ Increased costs due to the required investments
☑ New costs	☐ Other:	

Potential structural and organisational impact

Structural impact

The Epicor LP system should be used exclusively in cardiac surgery or hybrid theatres; it uses instruments which do not require structural changes. The control system does not occupy a sizeable space.

☑ Increase in requirement of instruments	☐ Always be used	☑ Can be used only under specific circumstances
☐ Decrease in requirement of instruments	☐ Other:	☐ Not identified

Organisational impact

The procedure must be carried out by a team made up of: a cardiac surgeon, an assistant surgeon and possibly a third operator plus a machine operator (usually a nurse). Team members must undergo 1-2 days' training in a centre recognized by the manufacturer (St. Jude Medical Inc).

☑ Increase in the number of procedures	☐ Re-organisation required	☑ Training required for users
☐ Reduction in the number of procedures	☐ Other:	☐ Not identified

Conclusions

Minimally invasive treatment for atrial fibrillation by HIFU ablation is an emerging technology in Italy and around the globe. The technology appears to have high potential for the treatment of AF in patients who are resistant to pharmacological therapies and/or have undergone unsuccessful transcatheter ablation.

HIFU ablation, when performed alongside other cardiac surgery procedures has shown itself to be safe and effective [CEDIT, 2006; Ninet, 2005; Groh, 2007]. The minimally invasive approach of Epicol LP is probably advantageous for access and reducing intra-operative risks. However given the limited number of cases that have undergone the procedure in Italy (10 people all in the same centre) further evidence is necessary before a recommendation for widespread use can be made.

The use of the procedure for treating isolated AF should undergo a risk-benefit analysis.

The minimally invasive approach for treating AF associated with the substitution or the repair of the mitral valve has already been put forward as an alternative to the same procedure carried out under open chest surgery conditions.

Future prospects

- Population: if the evidence shows its safety, the minimally invasive approach could be extended to a wider age group of patients (for example those with isolated AF).

- Intervention: the size of the device should remain the same in the future (current size is a compromise between ablation power and design limits); the system updates will chiefly enhance control system portability.

- Comparators: minimally invasive AF ablation systems using energy sources other than HIFU (e.g., cryoablation, lasers, microwaves and radio frequencies) and different access pathways (e.g., balloon catheters) will enter the market.

- Outcomes: the main outcomes of prospective studies should include atrial eurythmia resumption and thrombosis and embolism risk reduction.

Evidence searches

The searches were made using combination of the following terms: *atrial fibrillation; minimally invasive; ablation; ultrasound.*

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www.fibrillazioneatriale.it

www.sjm.com/

Glossary

AF: Atrial fibrillation

FDA: Food and Drug Administration

HIFU: high intensity focused ultrasound

HS: horizon scanning

Mini-thoracotomy: small incision in the intercostal space.

MLSPS: Italian Ministry of Labour, Health and Social Policies

NHS: National Health Service

RDM: Inventory of Medical Devices