Forfait Innovation

Towards a Fast Tracking of medtech innovations

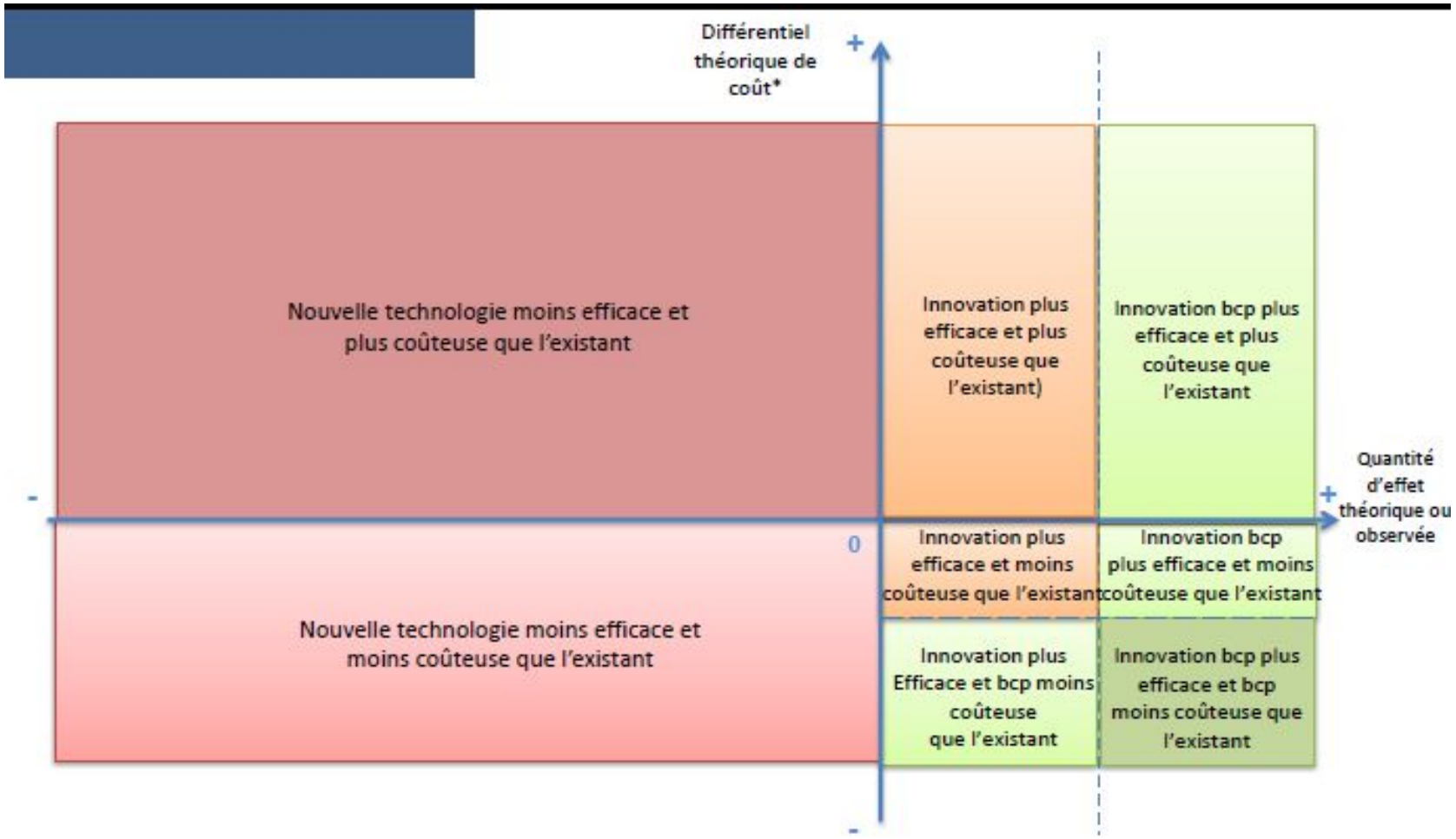
Le BelvédèrE

www.lebelvedere.team

Introduction

Framework and Objectives:

- Secured access for patients to disruptive innovations while monitored gathering of structured clinical and/or medico-economical missing data which enable later decision taking for more consistent healthcare support
- Exceptional and temporary reimbursement of an innovative medical device (MD-IVD) or act upon the condition that a study is conducted to collect missing clinical and/or economical data



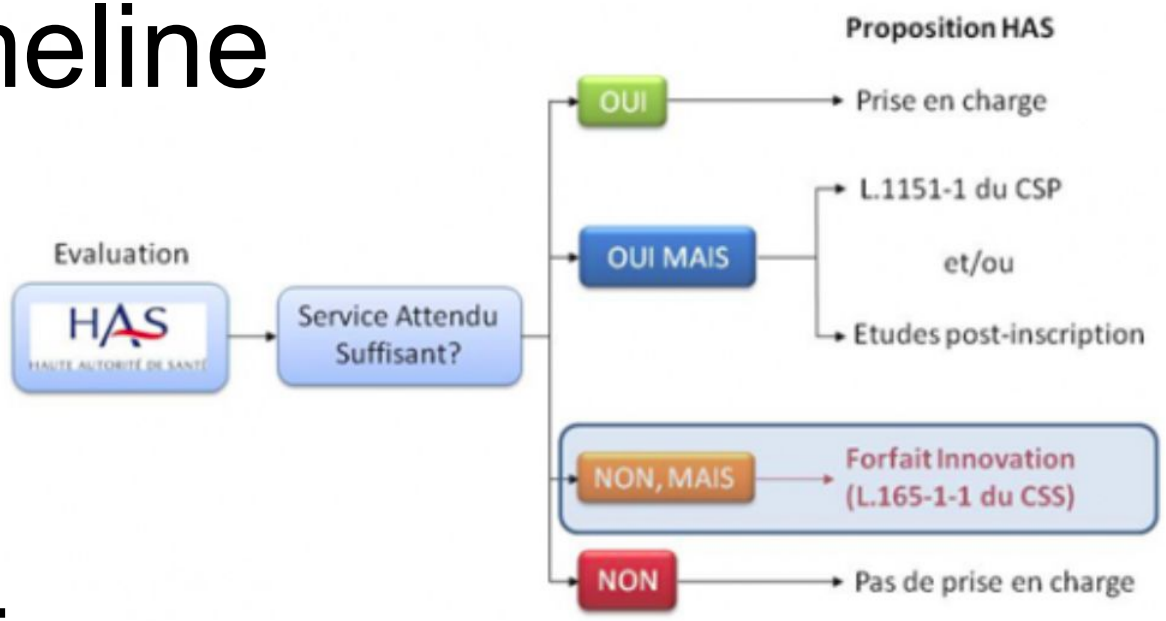
*: theoretical difference between usage costs of innovation and gold standard technique

Innovations eligible for forfait innovation

New technologies non eligible for forfait innovation (no in fine innovation)

Innovations non eligible for forfait innovation (but possible validation throught PHRC, PRME…research protocols)

Analysis timeline



- **Phase 0: Bid filing**
- **Phase 1: Initial analysis w.r.t eligibility criteria**
- **Phase 2: Feasibility evaluation of clinical study or medico-economics protocol**
- **Phase 3: Review by board of trustees (college)**
- **NB: Appeal possible within 2 months delay**

2/18/2015 Decree: *Dispositions relatives à la prise en charge des produits de santé ou actes innovants.*

1- Requester

- **Medical Device: Manufacturer or distributor, sometimes in association with Healthcare institutions, medical associations**
- **Acts: National Professional board**

2- Innovation criteria

- **Novelty level: disruptive (non incremental)**
  - **Relevant medical need or**
  - **Significant reduction of medical costs**
  - **EC Label**
  - **Low risks for patients**

3- On condition that a clinical or medico-economic trial is conducted (3–5 y.):

- **Gathering missing data to confirm the medical/economical benefits**
- **Sufficient expected benefit**

4- Procedure: Short delay and review (120 days max in total)

- **45 days for HAS**
  Admissibility – Review by Jury HU
  Decision of the collegium and if favorable
- **30 days for HAS & Ministery of Health**
  Statement on the relevancy and funding of the study
- **30 days for official clearance publication**

First candidates

- **Medico-surgical acts (n = 3):**
  - **– Right lobe Hepatectomy with *coelioscopy* for liver cancer**
  - **– Oesophagectomy with plasty by *thoracoscopy* for œsophage cancer**
  - **– Treatment of localized prostate adenocarcinoma with high intensity focused ultrasounds (ABLATHERM)**

- **Medical Devices (n =3):**
  - ***– PARADIGM VEO, continuous monitoring of interstital glucose level combined with an insulin pump***
  - ***– SIR-Spheres: yttrium-90 containing microspheres for selective internal radiotherapy***
  - **– ARGUS II, epiretinian implant**

- **Technology combining an act, a medical device and a drug:**
  - **– Autologous chondrocytes therapy with Chondrocelect.**

2 Examples

- ARGUS II (Second Sight Medical Products)
- Ablatherm (EDAP TMS)

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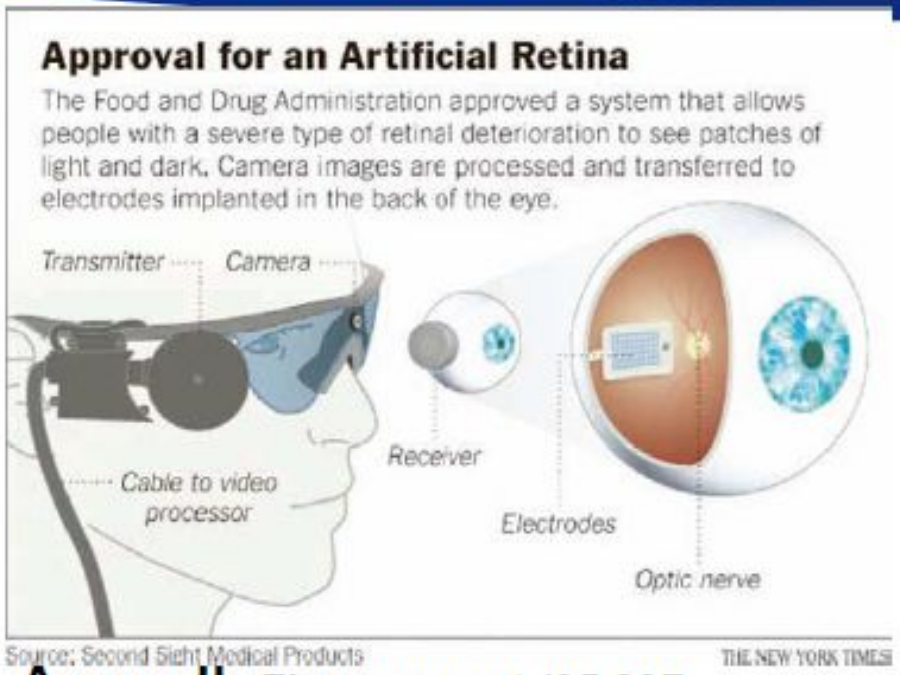


– **Argus II: Financement (95.897 euros/pts par l'assurance maladie durée de 5 ans avec étude sur 36 malades dans 3 centres.**

– **Ablatherm: Financement (6047 euros/pts) durée de 6 ans avec étude de 2500 patients dans 42 établissements.**

Primary objective: comparison of recurrence free survival (i.e. RDT or hormonotherapy rate) for patients undergoing first-line treatment vs. Radical prostatectomy.

Ablatherm HIFU

Ablatherm® (EDAP TMS, Lyon, France) HIFU (High Intensity Focused Ultrasounds) device has been developed since 1993 for the radical treatment of localized prostate cancer.

It is suitable for men who are at risk for surgery due to their age or other associated illnesses, or who may not want to undergo surgery.

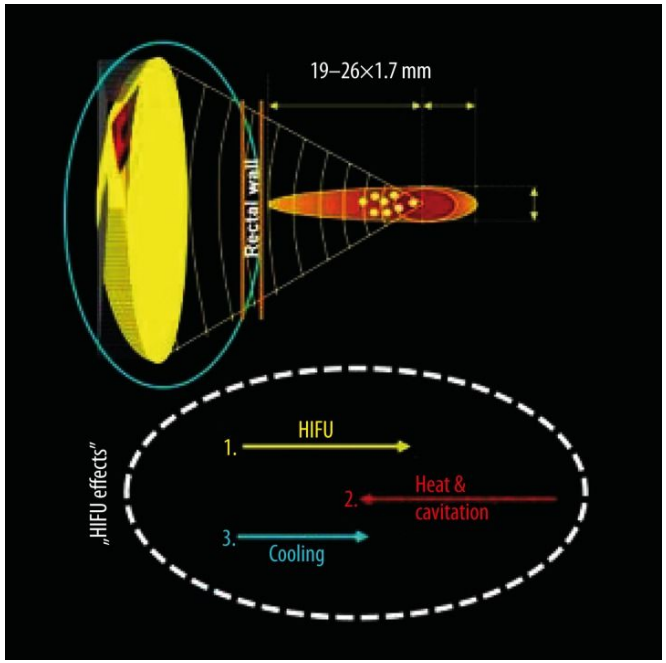
Main indications:

Patients older than 70 years, whose life expectancy exceeds 5 years (or younger patients with competitive morbidity) with localized stage T1- T2 NxM0 cancer, Gleason score ≤7 (3+3 & 3+4), PSA < 15 ng/ml, and limited tumoral volume.

Second line treatment after histologically proven local recurrence for patients treated with external radiotherapy

HIFU in a nutshell

- External high energy ultrasound beam focused on tumour target
- Absorption of energy: very localised temperature rise at focus
- Sharply demarcated volume of coagulative necrosis
- No damage to overlying and surrounding tissue



Pol J Radiol. 2015 Mar 13;80:131-41

Protocol

- 3D imaging (3D imaging of the prostate with 7.5 MHz transducer)
- Treatment planning (fully adjustable treatment parameters to suit all prostate anatomies)
- Robotic treatment (robotic treatment of the prostate following the treatment plan)
- At the point where the ultrasound waves are focused the absorption of the ultrasound beam creates a sudden temperature increase (around 85°C) which destroys the tissue in the targeted zone.

Prog Urol. 2011 Mar;21(3):191-7.

Outcomes of HIFU for localised prostate cancer using the Ablatherm Integrate Imaging® device.

Crouzet S1, Poissonnier L, Murat FJ, Pasticier G, Rouvière O, Mège-Lechevallier F, Chapelon JY, Martin X, Gelet A.

- **OBJECTIVES:**

  To report the functional and oncological outcomes of HIFU for prostate cancer using the Ablatherm Integrate Imaging(®) device.
- **METHODS:**

  Between January 2005 and June 2009, all patients treated with HIFU as a primary care option for localized prostate cancer and fulfilling the French Urological Association (AFU) guideline were included in this study. Validated questionnaires were used to assess continence, potencies and quality of life.
- **RESULTS:**

  A total of **297 patients** met the inclusion criteria: 149 were low risk and 148 were intermediate risk according to d'Amico's risk group. The median prostate specific antigen (PSA) nadir was 0.12ng/ml with 65% of patients reaching a nadir less than 0.3 ng/ml. Systematic control biopsies were performed on 175 patients with 89% of negative biopsies. The disease free survival rate at 40 months was 79% for low risk group and 62% for intermediate risk group. The pre and post-HIFU treatment International Prostate Symptoms Score (IPSS) score and quality of life questionnaire were not statistically different. In the opposite, the pre and post-HIFU erection function and continence status were significantly different.
- **CONCLUSION:**

  Local control and Biochemical Free Survival Rate achieved with HIFU were similar to those expected with conformal external radiation beam therapy. Among the functional outcomes, potency was the most impacted by the treatment.

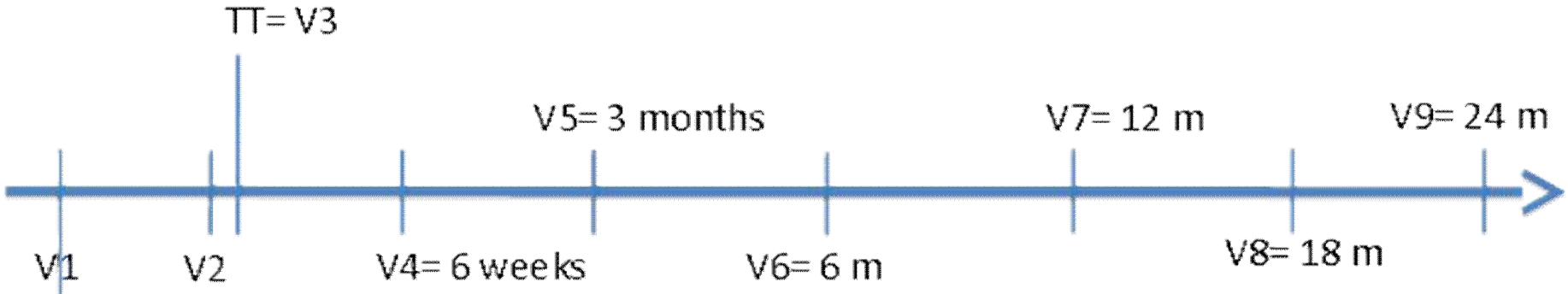
Forfait innovation Study design

- **Methodology** : Open non-randomized follow-up prospective cohort study, multicentric,
- **Planning**: 2.5 years inclusion + 2.5 years follow-up
- **Number of patients**: 20 first-line patients minimum / y./ center plus 10 salvage patients minimum / y./ center after radiotherapy, hence more than 2500 patients.
- **Number of centers**: 42 (private / public / PSPH)
- **Costs**: more than 20 M euros for surgery plus more than 1M euros.

Funding: 6 047 euros per patient for the medical centers

Follow-up

PSA: V4 to V12
PBP if PSA > 1ng/ml at V6 or if nadir +2ng/ml
IPSS, Ingelman-Sundberg, QLQ-C30, IIEF5: V6, V7, V9-V12



V1
Clinical
Biology
Q? (IPSS, Ingelman-Sundberg, QLQ-C30, IIEF5)
Echo, MRI
(scinti)

V10= 3 years
V11= 4 years
V12= 5 years

Argus II

- **Argus II Retinal Prosthesis System** intended to provide electrical stimulation of the retina to induce visual perception in blind individuals.
- An epiretinal prosthesis surgically implanted in and on the eye that includes an antenna, an electronics case, and an electrode array.
- The external equipment includes glasses, a video processing unit (VPU) and a cable

CNEDiMTS Position paper on ARGUS II, Novembre 20th 2012

Indications revendiquées :	Patients : • ayant un âge supérieur ou égal à 25 ans ; • souffrant de dégénérescence rétinienne externe sévère à profonde ; • bénéficiant d'une perception résiduelle de la lumière. S'il n'existe aucune perception résiduelle de la lumière, la rétine doit être capable de répondre à une stimulation électrique ; • ayant une acuité visuelle limitée au « décompte des doigts » ou inférieure au niveau des deux yeux (2,0 LogMAR ou pire) ; • ayant eu une vision utile des formes dans le passé.
Service Attendu (SA) :	**Insuffisant** L'intérêt du produit ne pouvant être établi au vu des données fournies dans le dossier médico-technique. **Cependant, la CNEDiMTS souligne qu'il est indispensable d'encourager et de soutenir le recueil de données cliniques complémentaires en vie réelle par le biais d'études bien conduites compte tenu du fort potentiel de cette technologie innovante qui permettrait de compenser le handicap de patients ayant une cécité induite par une pathologie rare et pour laquelle il n'existe aucun traitement à ce jour.**

Données analysées :	***Une étude de faisabilité, prospective, multicentrique, non comparative portant sur 30 patients avec un suivi minimum de 1 an a été retenue. L'objectif était d'évaluer la sécurité et l'efficacité de la prothèse épirétinienne ARGUS. Les critères de jugement principaux de sécurité et d'efficacité étaient respectivement le recensement des évènements indésirables (graves et non graves) et l'évaluation de l'acuité visuelle.***

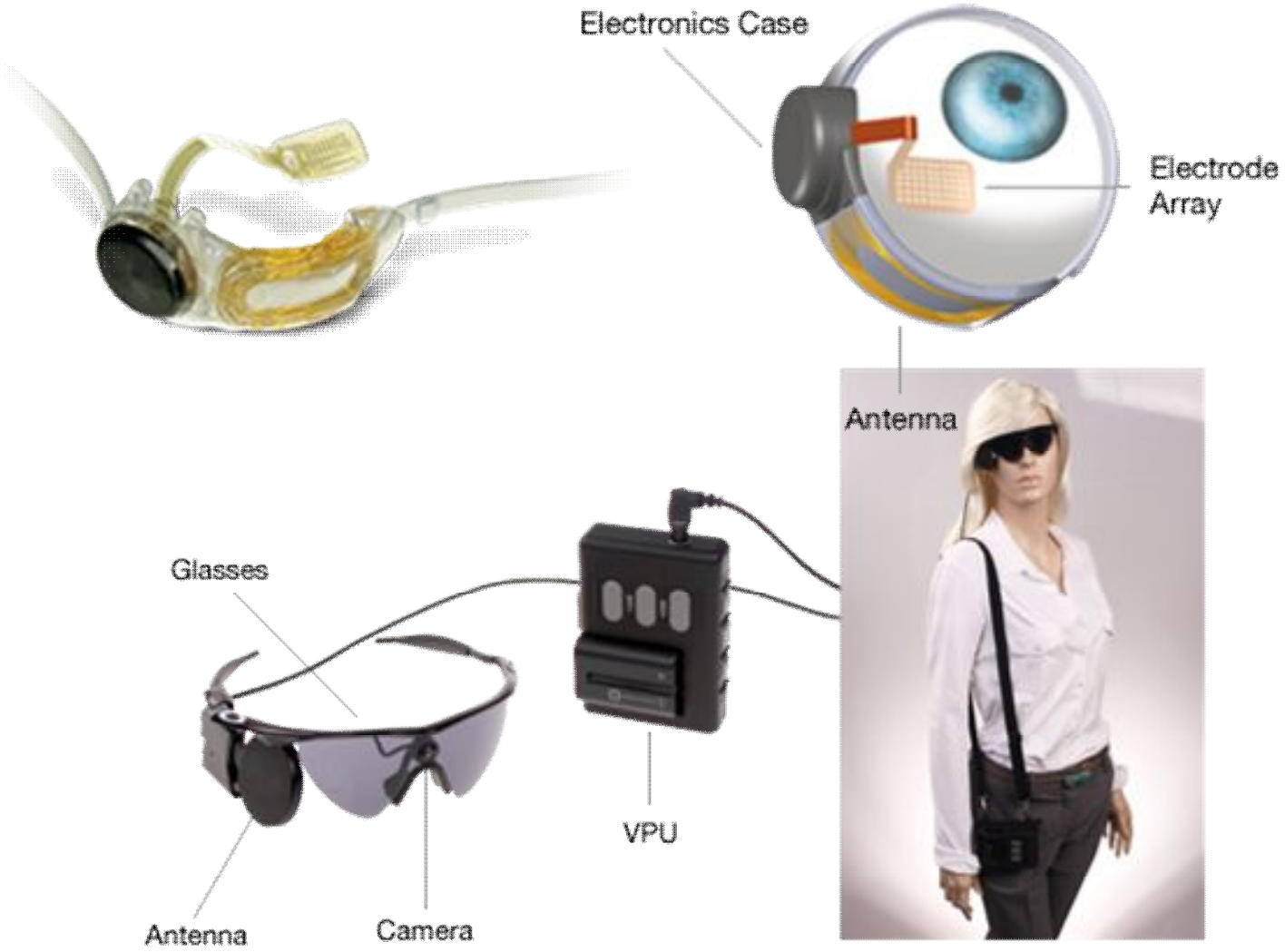
Retinitis Pigmentosa (RP)

- In a healthy eye, the **photoreceptors (rods and cones) in the retina convert light into tiny electrochemical impulses** that are sent through the optic nerve and into the brain, where they are decoded into images.
- Disease that leads to **degeneration of the rods and cones of the retina**; One of the leading causes of inherited blindness. Symptoms may appear at adolescence, but severe vision problems do not normally occur before early adulthood. In the early stages of the disease, people with RP experience **loss of night vision and more difficulty seeing in low-light conditions**. As the disease progresses, RP sufferers begin to lose peripheral vision and develop '**tunnel vision**'. In the most advanced stages, a person with RP may become completely blind.
- Other forms of RP and related diseases include Usher syndrome, Leber's congenital amaurosis, rod-cone disease, and Bardet-Biedl syndrome, among others.

Candidates

- Adults, age 25 years or older
- Severe to profound outer retinal degeneration
- Some residual light perception; if no residual light perception remains, the retina must be able to respond to electrical stimulation
- Previous history of useful form vision
- CNEDIMTS clearance in September 2017

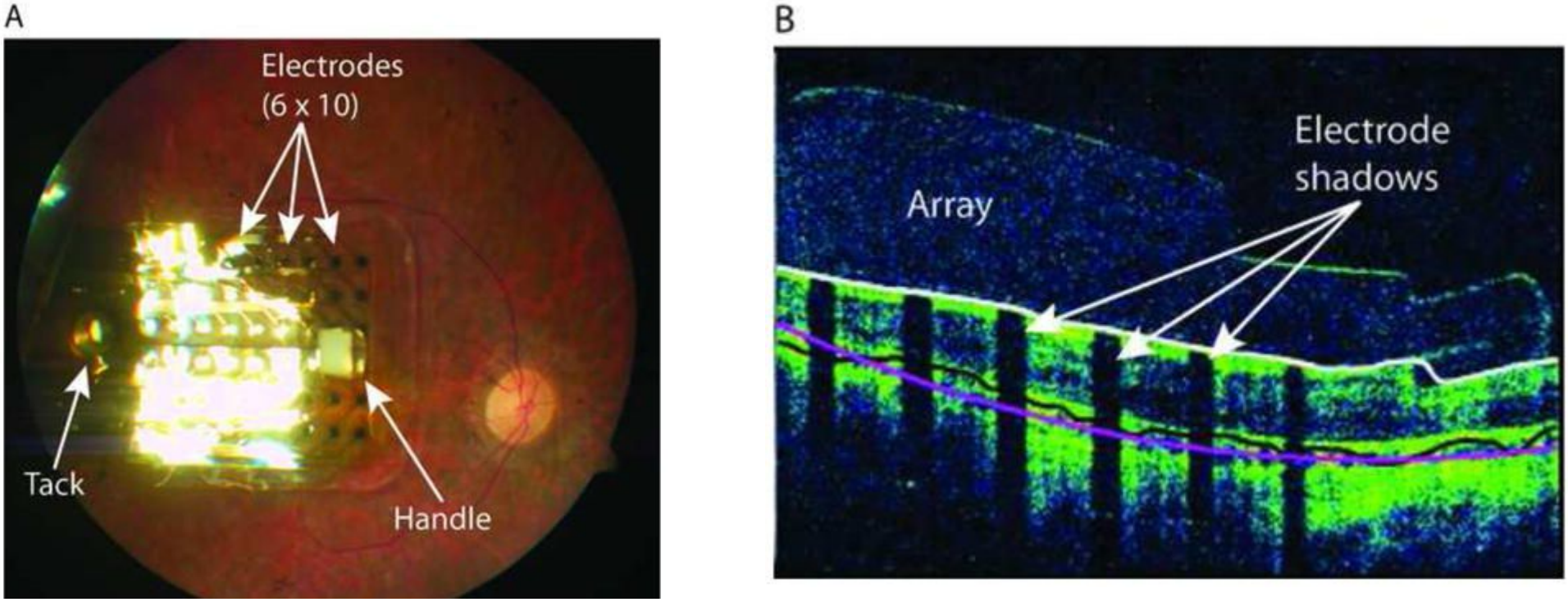
Technology


Electronics Case
Electrode Array
Antenna
Glasses
VPU
Antenna
Camera

Ophthalmology. 2012 Apr; 119(4): 779–788.

(A) Fundus photograph of implanted Argus II array in the macular region. The electrode array is secured to the retina with a retinal tack; the white square visible on the distal side of the array is an opaque section of tubing (the “handle”) used by the surgeon to position the array.

(B) (B) An optical coherence tomography (OCT) image of an implanted Argus II array. Shadows cast on the retinal image (white arrows) are due to occlusion of the scanning light source by the metal electrodes.



Long-Term Results from an Epiretinal Prosthesis to Restore Sight to the Blind

- **PURPOSE: Retinitis pigmentosa** (RP) is a group of inherited retinal degenerations leading to blindness due to photoreceptor loss. RP is a **rare disease**, affecting only approximately 100 000 people in the US. There is no cure and no approved medical therapy to slow or reverse RP. The purpose of this clinical trial was to evaluate the **safety, reliability, and benefit** of the Argus II Retinal Prosthesis System in restoring some visual function to subjects completely blind from RP. We report clinical trial results at 1 and 3 years after implantation.
- **DESIGN:** multicenter, single-arm, prospective clinical trial.
- **PARTICIPANTS:** 30 subjects in 10 centers in the United States and Europe. Subjects served as their own controls, that is, implanted eye versus fellow eye, and system on versus system off (native residual vision).
- **METHODS:** The Argus II System was implanted on and in a single eye (typically the worse-seeing eye) of blind subjects. Subjects wore glasses mounted with a small camera and a video processor that converted images into stimulation patterns sent to the electrode array on the retina.
- **MAIN OUTCOME MEASURES:** The primary outcome measures were safety (the number, seriousness, and relatedness of adverse events) and visual function, as measured by 3 computer-based, objective tests.
- **RESULTS:** A total of 29 of 30 subjects had functioning Argus II Systems implants 3 years after implantation. Eleven subjects experienced a total of 23 serious device- or surgery-related adverse events. All were treated with standard ophthalmic care. As a group, subjects performed significantly better with the system on than off on all visual function tests and functional vision assessments.
- **CONCLUSIONS:** The 3-year results of the Argus II trial support the long-term safety profile and benefit of the Argus II System for patients blind from RP. **Earlier results from this trial were used to gain approval of the Argus II by the FDA and a CE mark in Europe**. The Argus II System is the first and only retinal implant to have both approvals.
- **Ophthalmology. 2015 Jul 7th**

RESEARCH ARTICLE Open Access

The cost-effectiveness of the Argus II retinal prosthesis in Retinitis Pigmentosa patients

Anil Vaidya[1*], Elio Borgonovi[2], Rod S Taylor[3], José-Alain Sahel[4], Stanislao Rizzo[5], Paulo Eduardo Stanga[6], Amit Kukreja[7] and Peter Walter[8]

Abstract

Background: Retinitis Pigmentosa (RP) is a hereditary genetic disease causing bilateral retinal degeneration. RP is a leading cause of blindness resulting in incurable visual impairment and drastic reduction in the Quality of life of the patients. Second Sight Medical Products Inc. developed Argus II, a retinal prosthesis system for treating RP. Argus II is the world's first ever-commercial implant intended to restore some vision in the blind patients. The objective of this study was to assess the cost-effectiveness of the Argus® II Retinal Prosthesis System (Argus II) in Retinitis Pigmentosa (RP) patients.

Method: A multi -state transition Markov model was developed to determine the cost-effectiveness of Argus II versus usual care in RP from the perspective of healthcare payer. A hypothetical cohort of 1000 RP patients aged 46 years followed up over a (lifetime) 25-year time horizon. Health outcomes were expressed as quality adjusted life years (QALYs) and direct healthcare costs expressed in 2012 €. Results are reported as incremental cost per ratios (ICERs) with outcomes and costs discounted at an annual rate of 3.5%.

Results: The ICER for Argus II was €14,603/QALY. Taking into account the uncertainty in model inputs the ICER was €14,482/QALY in the probabilistic analysis. In the scenarios of an assumption of no reduction on cost across model visual acuity states or a model time horizon as short as 10 years the ICER increased to €31,890/QALY and €49,769/QALY respectively.

Conclusion: This economic evaluation shows that Argus II is a cost-effective intervention compared to usual care of the RP patients. The lifetime analysis ICER for Argus II falls below the published societal willingness to pay of EuroZone countries.

Keywords: Retinitis Pigmentosa, Retinal prosthesis, Cost-effectiveness analysis, Decision analytic modelling

Last clearances

- Nov. 2017, **METAglut1** (METAFORA biosystems) to measure the expression level of GUT1 transporter on the erythrocytes surface -> indicated for GLUT1-DS, rare neuro-metabolic disease

  -> less invasive and equivalent diagnostic performances as compared to glycorachie?
- Sept. 2017, **Argus II**
- Sept 2017, **Retina Implant Alpha AMS**, same ,indications as compared to Argus II: peripherical retinal degeneration w/wo residual visual perception of light and an history of usefull vision

- Dec. 2016, **Echopulse**, Theraclion: treatment of breat fibradenoma with HIFU. 1.5 years procedure delay.

References

- https://www.has-sante.fr/portail/jcms/c_2035788/fr/forfait-innovation
- http://solidarites-sante.gouv.fr/systeme-de-sante-et-medico-social/recherche-et-innovation/forfait-innovation
- https://www.has-sante.fr/portail/upload/docs/application/pdf/2017-09/forfait_innovation_procedure.pdf
- Article L. 165-1-1 du code de la sécurité sociale : **https://tinyurl.com/y8xtnltp**
- Décret du 16 février 2015: **https://tinyurl.com/ycagla4u**
- Circulaire du 4 septembre 2015 : **https://tinyurl.com/y78alesf**