Restoration of Sight in Geographic Atrophy using a Photovoltaic Subretinal Prosthesis

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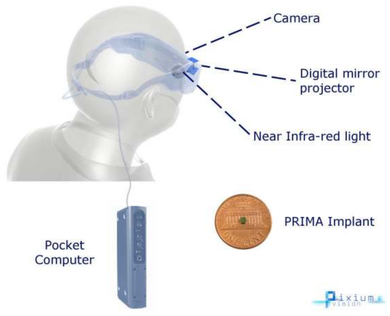

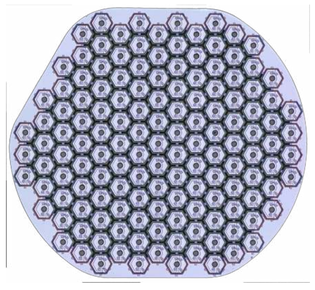

2 mm² PRIMA photovoltaic subretinal microchip

OBJECTIVE: To evaluate feasibility of restoration of central vision in patients with age-related macular degeneration using a wireless photovoltaic subretinal implant. In particular, to assess safety of sub-retinal implantation and quality of prosthetic vision in patients with geographic atrophy.

MATERIAL-METHODS: A prospective study in 5 patients with visual acuity ≤20/400 due to geographic atrophy of at least 3 optic discs diameters and no foveal perception. Wireless photovoltaic chip (PRIMA, Pixium Vision) is 2x2mm in size,30µm in thickness, containing 378 pixels of 100µm in width. Each pixel converts pulsed near-infrared light (880nm) projected from video-goggles into electric current to stimulate nearby neurons in the inner retina nuclear layer. Several surgical techniques used, varying in anesthesia (local vs. general) and retinal reattachment (gas vs. oil)

RESULTS: In all patients, surgery lasted approximately 2 hours, chip was successfully implanted under the macula and remains stable, with a follow-up extending now to 11 months in first patient. In 3 patients chip was placed into a desired position-centrally and close to the inner retina. In 2 patients the implant ended up in suboptimal positions–one in the choroid and another off-center. All 5 patients perceive white-yellow patterns with adjustable brightness, in retinotopically correct locations within previous scotomata. No decrease in natural visual acuity was observed in any patient. All 4 patients with subretinal chip placement correctly identify bar orientation, with 93.5+/-3.8% accuracy. Out of them, all 3 patients with central placement of the implant demonstrated visual acuity with Landolt C test in the range of 20/460-20/550,which is just 15-35% below the theoretical resolution limit for this pixel size (20/400).Patients are now being tested in letter recognition, reading, and other visual tasks.

CONCLUSIONS: Wireless chip PRIMA can be safely implanted under the atrophic macula in patients with geographic atrophy and restore central visual perception with acuity close to the theoretical limit of the implant. Implantation did not reduce the natural residual visual acuity of the patients. Implants with smaller pixels are being developed.

PRIMA, Human feasibility studies in patients blind from Advanced dry-AMD

FEASIBILITY STUDIES

Feasibility Study of Compensation for Blindness With the PRIMA System in Patients With Dry Age Related Macular Degeneration

CRITERIA
- 60 years or older
- Visual Acuity of LogMAR 1.3 (20/400) or worse
- No foveal perception

PRIMARY ENDPOINT
Elicitation of visual perception with PRIMA implant and safety assessment after implantation.

PRIMA-FS ClinicalTrials.gov
5 patients implanted in France
Recruitment closed
Positive 6 months data available
CLINICAL SITES
Dr. Yannick Le Mer
Fondation Ophtalmologique Adolphe de Rothschild
QUINZE-VINGTS

PRIMA-FS-US ClinicalTrials.gov
5 patients in USA – Recruitment open
Safety assessment at 12 month after implantation
UNIVERSITY OF PITTSBURGH MEDICAL CENTER
Pr. José Sahel – Dr. Joseph Martel
UPMC LIFE CHANGING MEDICINE

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French Study Inclusion criteria

Feasibility Study of Compensation for Blindness With the PRIMA System in Patients With Dry Age Related Macular Degeneration
Open-label, non-randomized

The intended use of the PRIMA System is for the restoration of limited visual perception in patients suffering from atrophic advanced dry Age related Macular Degeneration.

- The key-inclusion criteria imply that the patient:
  - Is 60 years or older at the date of inclusion;
  - Has a confirmed diagnosis of advanced dry age related macular degeneration with an atrophy size of at least 3 optic disc diameters;
  - Has best corrected visual acuity in the study eye of logMAR 1.3 (20/400) or worse measured by ETDRS;
  - Has no foveal perception measured by micro-perimetry in the study eye;
  - Has a refraction of study eye between –3 and + 4 (limits included) for patients with IOL (there is no refraction criteria for patients with natural lens);
  - Understands and accepts the obligation to present for all schedule follow-up visits.

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Demographic overview at inclusion

Patient	P1	P2	P3	P4	P5
Age/Sex	83/F	66/F	82/M	69/M	74/M
logMAR	1.3	>1.6 (HM)	>1.6 (CF)	1.4	1.4
Atrophy size [mm2]	13.6	20.7	17.1	15.4	23.4
Diagnosed	2011	2013	2014	2013	2004
Implanted eye	left	left	left	right	left
Implantation	12 Dec 2017	19 Dec 2017	20 Feb 2018	5 Jun 2018	27 Jun 2018

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Clinical performance in human at 6 months exceeded initial expectations

- **5 patients** successfully implanted in France
  - **Elicited visual perception** in degenerated central retina with no activity
  - Progressively identifying letters and sequence of letters
  - Patient training and follow-up currently spans 8 to 14 months
- **Safety** profile
  - No implant-related serious adverse events
  - Transitory procedural complications resolved
  - **Preservation of peripheral remaining natural visual acuity**

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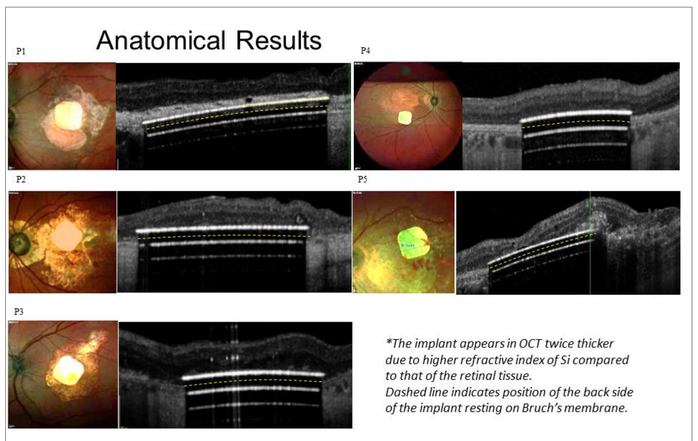
Anatomical Results



**The implant appears in OCT twice thicker due to higher refractive index of Si compared to that of the retinal tissue. Dashed line indicates position of the back side of the implant resting on Bruch's membrane.*

- Subretinal implantation of the wireless PRIMA chip in atrophic dry AMD is feasible and safe.

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PRIMA Safety results at 6 months

- One serious adverse event (SAE) due to missed administration of standard medication post implant
- 18 procedure or device related non serious adverse events (NSAEs)

- Overall safety status considered excellent
- The number of non-serious / minor adverse events expected to be reduced by improving the surgical delivery tool and technique

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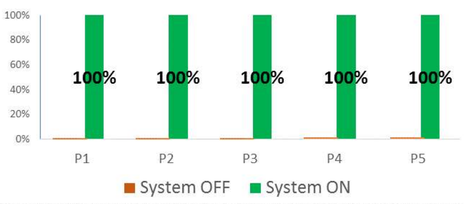
PRIMA Primary endpoint: Elicitation of light perception measured* with system on and off

Patient ID	Nb de perception/Nb de stimulation	
	Système « Off »	Système « On »
P1	0/5	5/5
P2	0/5	5/5
P3	0/5	5/5
P4	0/5	5/5
P5	0/5	5/5

Method:
- VPM mode (computer generated pattern)
- Stimulus 10-20 seconds
- Full field



*performance of the chip and system without use of peripheral remaining vision (measures only with fully opaque glasses)

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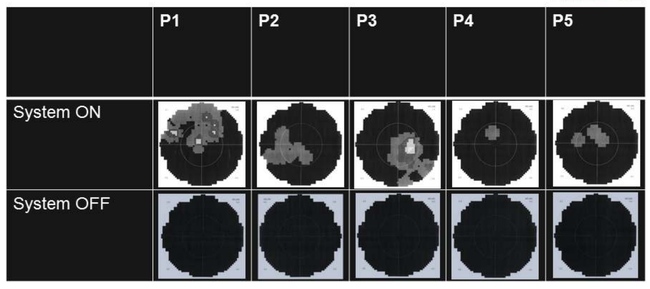
PRIMA central visual perception at 6 Months

- Octopus Visual Field Measurement*
- Fully opaque glasses: light perception via PRIMA chip only



*performance of the PRIMA chip and system without use of any peripheral remaining vision (only with fully opaque glasses)

Corporate Presentation - February 2019
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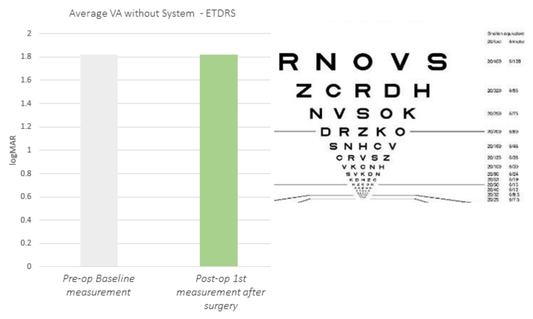
Visual acuity (ETDRS) Pre vs Post implantation



PRIMA can be safely implanted under the atrophic macula while preserving the residual natural peripheral visual acuity, measured via ETDRS

PRIMA performance and prosthetic vision tests : Landolt C Acuity*

Acuity measured with Landolt C
- Theoretical limit with 100µm pixels
  - 20/400 (1.30 logMAR), 1.0 pixel
- Mean Acuity obtained with PRIMA**
  - 20/500 (1.40 logMAR), 1.23 pixels
- Best visual acuity obtained with PRIMA
  - 20/460 (1.37 logMAR), 1.15 pixels

15-35% below the theoretical limit of resolution for 100 µm pixels

	PRIMA	Alpha IMS/AMS***
Best acuity	1.366 logMAR	1.44 logMAR
Patients scoring	3/5	2/60
Residual vision	Not yet used	Fully used

- *Performance of the chip and system without use of peripheral remaining vision (measures only with fully opaque glasses)
- ** Mean visual acuity of 20/500 when chip is placed directly under the retina closed to the fovea
- *** Stingl et al.2017 Frontiers in neurosciences

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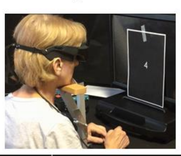
Letter recognition Patient case study*

Method:
- Two subsets of letters are presented (A and B)
- Letter size 3.5 cm, 30 cm distance
- White letters on black background



PRIMA (one patient at 6 months)	Set A (32 trials) [EFHIJLTU]	Set B (40 trials) [ZVWMOQCNDV]
CORRECT ANSWERS (%):	68.75	72.5
AVERAGE TIME FOR CORRECT ANSWERS (s):	7.63	13.44

* Performance of the chip and system without use of peripheral remaining vision (measures only with fully opaque glasses)

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Conclusions

- Subretinal implantation of the wireless PRIMA microchip in atrophic dry AMD is feasible and safe.
- No decrease in residual natural vision compared to pre-operative visual acuity.
- ALL 5 patients reached the functional primary end point of the feasibility study (visual light perception in the former scotoma).
- PRIMA provided the best prosthetic visual acuity to date: 20/460 – only 15% below the theoretical limit for 100µm pixels.
- Most subjects recognize complex patterns close to the theoretical limit of the implant resolution.

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