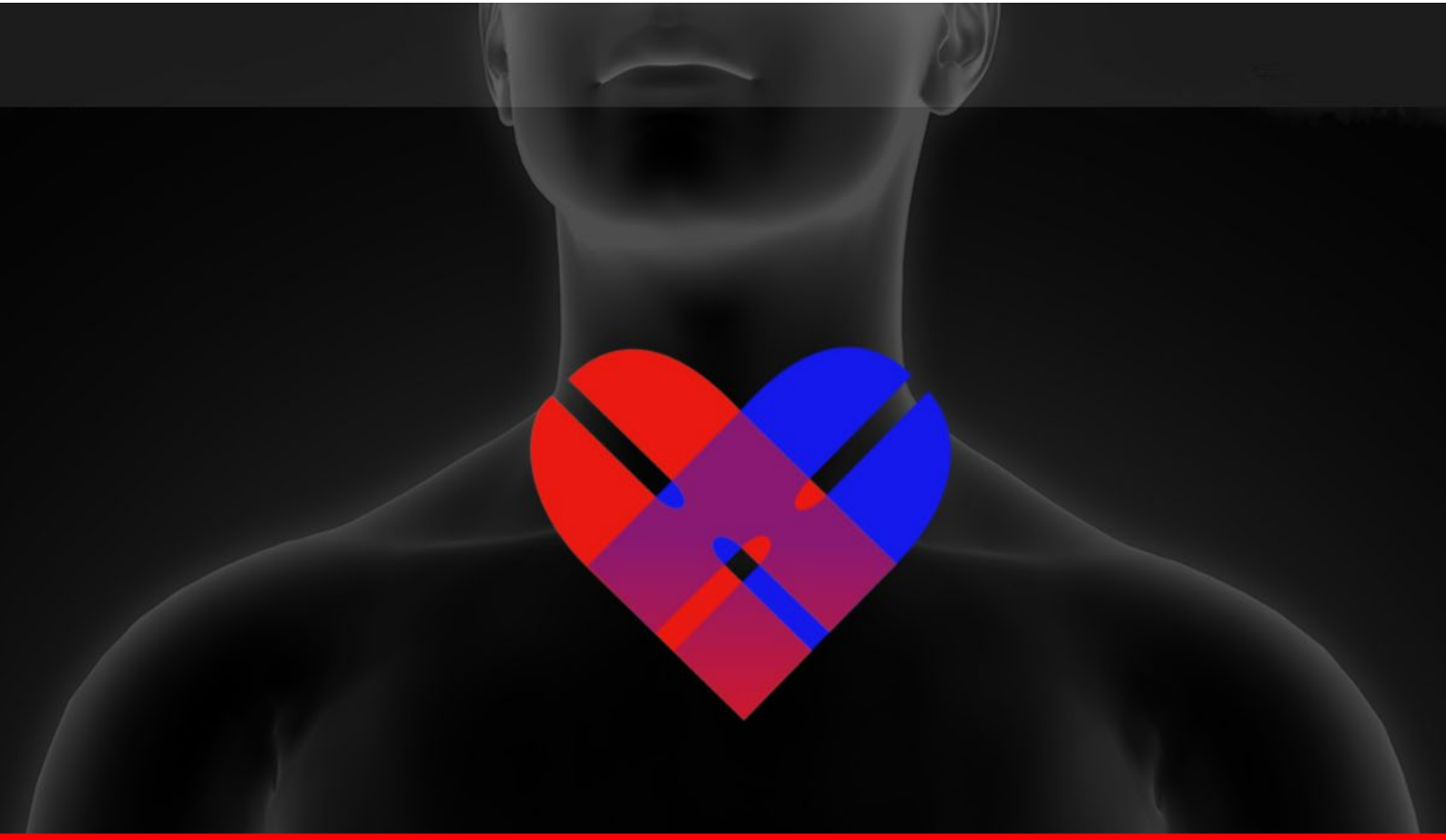

HYBRIDHEART

White paper on requirements and constraints of combining technologies

A unique solution for the all unsolved ones

Every year worldwide 26 million people die because of heart failure. In Europe, 45% of the overall number of deaths is related to cardiovascular diseases. Despite all the technological advances, no final and optimal solution to the problem has been found yet. Indeed, heart transplantation is still the only way to guarantee a normal life to the end-stage patients. For these reasons, the HybridHeart project aims to develop an alternative solution to the already available ones, trying to combine the power of the soft robotics actuation, the advances in tissue engineering and the farsighted ideas of transcutaneous energy transfer systems, to guarantee biomimetism, biocompatibility and lower the risk of infections.

Our Goals.

The main aim of this document is to integrate all the known physiological requirements, and all the expected technological constraints, that we consider to be needed decision-making factors during the development of an innovative generation of total artificial hearts. In every section. we tried to, not only present our main design goals, but also position them with respect to the ones characterizing the already developed, and sometimes commercialized, total artificial hearts.

THE SYSTEM OVERVIEW

General considerations

The envisioned system will be composed of a soft robotics shell, able to replicate as closely as possible the natural cardiac functionality.

The motion, and thus, the pattern of actuation activation will be generated by an innovative typology of valves, made of soft materials. To function, an implantable source of continuous air supply will be needed.

The energy will be delivered internally through a (TET) system, i.e. a system able to transfer energy transcutaneously: the absence of percutaneous drivelines is essential when aiming to reduce the number of possible post-implant complications, as for example infections. Moreover, the TET technology will give to the patient the possibility to move freely, and complete autonomously tasks that would otherwise require help, as showering. This would be possible thanks to the presence of an internal secondary power supply, guaranteeing the correct functionalities also in case of emergency, with an energy support of up to 45 min, when at maximum charge.

Figure 1 System overview

HybridHeart will be able to pump physiological volumes of blood, against the natural cardiovascular system pressures through biocompatible valves, designed, as the ventricular shapes, to guarantee the best achievable fluidodynamics performances. These features, combined with the tissue engineered inner linings, will aim for making this innovative soft artificial heart, one of the best solutions for end-stage heart failure patients.

PHYSIOLOGICAL REQUIREMENTS

Stroke volume, pressures, frequency

In accordance with the performance goals described by the National Heart Lung and Blood Institute (NHLBI)[1] our Hybrid Heart should be capable of supporting the circulation with a left side output of 8 L/min without having to exceed a pump rate of 120 beats per minute while pumping into a mean systemic arterial pressure of 110mmHg and a mean pulmonary pressure of 20 mmHg. Furthermore, the aim of our HybridHeart is to provide potential for five years implantable tether-free operation within the human body.

Physiological cardiac output in a healthy human body

In resting conditions, the human heart beats approximately 75 beats per minute with a stroke volume of 70 ml per beat and an ejection fraction of 60%. This leads to a cardiac output of approximately 5 L/min in adults. In healthy individuals, the afterload in the aorta is about 80 mmHg, the afterload in the pulmonary trunk is about 10 mmHg, the right atrial pressure is about 0 mmHg and the left atrial pressure is between 1-5 mmHg. During exercise, the heart beat can increase to 150 bpm in healthy individuals and the stroke volume can increase to 130 ml. Note, however, that these values should be taken into account just as reference, since they can vary greatly between individuals[2,3].

Physiological cardiac output in the HybridHeart

The HybridHeart should be able to meet hemodynamic demands in individuals with a healthy mean systemic pressure during rest and light exercise, as well as in individuals with high blood pressure and high cardiovascular resistance. Therefore, we are aiming to develop a system that is able to a generate cardiac output between 5-8 L/min against aortic afterloads up to 110 mmHg. In order to reach this output, the HybridHeart will have a stroke volume between 35-80 ml and will operate at a frequency in a range of 60-120 bpm.

TIME TO COMPARE...

Description	Cardiac Output	Bpm	Stroke volume
SynCardia[4]	6-8 L/min	60-80	50/70 ml
AbioCor[5]	4-8 L/min	110-140	55 ml
CARMAT[6,7]	2-9 L/min	35-150	65 ml
ReinHeart[8]	4-7.5 L/min	95-155	60 ml
softTAH[9]	1-4 L/min	60-120	83/144 ml
HybridHeart	2-8L/min	60-120	35-80ml

TECHNOLOGICAL REQUIREMENTS

Energy use and Transcutaneous Energy Transfer

To design an energy transfer system able to supply in all conditions the HybridHeart total artificial heart, some considerations regarding the possible energy use of the entire system were advanced.

Indeed, since the power output of the HybridHeart should be available any time, also when the system is on internal power supply, information about the range of the power values to be transferred is needed. To do so, we started the computations from the knowledge that the fluidic output of the system, given the physiological requirements, will have to be between 1 W and 2.3 W, see "To clarify" box for more details. At this point, we considered as target efficiencies at the various stages of the energy transfer process:

- ✓ Fluidic input to HH → Fluidic output to blood
  η=15%
- ✓ Transfer efficiency pump → HH
  η=90%
- ✓ Electrical input to pump driver → Fluidic output to HH
  η=50%
- ✓ Total efficiency inside body (i.e., excluding TET)
  η=6.75%

TO CLARIFY

A stroke volume of 5L/min against 80 mmHg systemic and 10 mmHg pulmonary results in 1 W. In the same way, a stroke volume of 8 L/min against 110 mmHg systemic and 20 mmHg pulmonary results in 2.3 W.

Then, the required maximum power input to the pump (approx. size 130x130x100mm) driving electronics is:

$$P_{in} = \frac{P_{out}}{\eta} = \frac{2.3\ W}{0.0675} = 34W$$

Where P_{in} is the input power, P_{out} is the output power and η is the evaluated efficiency. This means that the available battery capacity should then be:

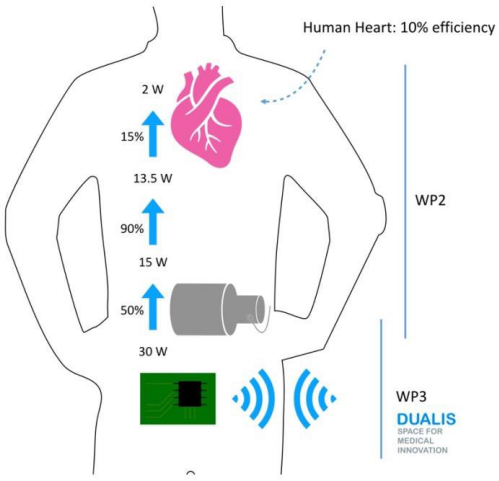

Figure 2 Power considerations

$$P_{in} \cdot \Delta t(hours) = 34W \cdot 0.75h = 25.5\ Wh$$

Typically, the available battery size is specified at least 20% more than the required available capacity, leading to an internal battery capacity of 31 Wh. Using the lower end of typical values for Li ION batteries, size and weight follow as specified in the next "Time to compare" table.[10,11]

Given these specifications, the TET system was designed. Note that particular attention, during the design phase will be given to the heating dissipation, in order to maintain the system at an acceptable physiological temperature.

TECHNOLOGICAL REQUIREMENTS

Energy use and Transcutaneous Energy Transfer

Given the evaluated power values, a TET system was designed. The main working principle will very similar to the one of the already developed TET used for supplying total artificial hearts. The energy is transferred through the coupling of two coils, one external, while the other internal to the body. The position of the system is envisioned to be in the infraclavicular region. The other electronics that will need to be implanted, will be, on the other hand implanted in the abdominal region.

In the following table our design is compared mainly to the one of the ReinHeart one, since there are no information about AbioCor, while Syncardia and CARMAT don't have one, since their supply has percutaneous drives.

Example of implantation locations can be associated to the ones declared for the AbioCor total artificial heart, Fig.3.

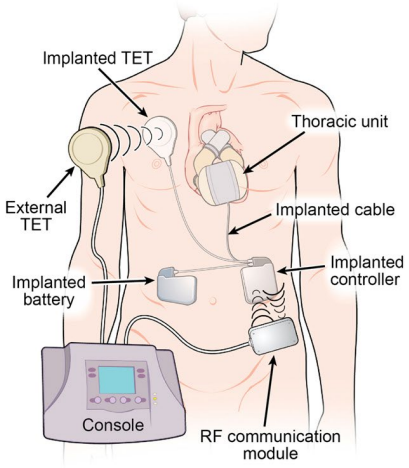

Figure 3 Abiocor TET system

TIME TO COMPARE...

Description	Coils dimensions	Batteries Weight	Internal batteries size	Location
Syncardia	--	--	--	--
AbioCor [5]	NA	NA	as defibrillators in size	Infraclavicular region
CARMAT	--	--	--	--
ReinHeart [8]	Internal 70mm External DO 100mm, DI 70mm Misalignment 30mm	Ext 2kg Int NA	NA	Infraclavicular region
HybridHeart	Internal 80mm External 100mm Misalignment 30mm (axial) 20mm (radial)	Int 300g Ext ≈2kg	125 cc	Coils in infraclavicular + in abdominal region.

TECHNOLOGICAL REQUIREMENTS

Space, weight, shape and modes of operation

The HybridHeart will be designed to fit in the majority of patients in need for a TAH, which means that the HybridHeart TAH aims to fit both in large man as well as in small men and women. Therefore, we will try to develop a device suitable for individuals of a BSA≥1.2 m^2, as the latest Syncardia model (50 cc)[12].

In general, however, due to the challenging nature of this requirement, it would be a great achievement for the consortium to de able to develop as first HybridHeart prototype, a total artificial heart implantable in the majority of male patients (BSA≥1.7 m^2, cardiothoracic ratio 0.5, anterior-posterior chest distance ≥100 mm, and a left ventricular diastolic diameter higher than 66 mm). Moreover, our goal is to make our design as light in weight as possible, considering a weight of 900gr as the maximum value for the intra-thoracic unit, as CARMAT CTAH[7].

TO CLARIFY

$$BSA\ (m^2) = \sqrt{\frac{Height(cm) \cdot Weight(kg)}{3600}}$$

For what concerns the shape, our device will be implanted as substitute of the natural and damaged ventricles. Moreover, with respect to the other available devices, HH will be pneumatic and its flow will be pulsatile.

TIME TO COMPARE…

Description	Modes of operation	Type of pump	Weight	Shape
SynCardia[4]	Pulsatile	Pneumatic	160 g	Ventricles
AbioCor[5]	Pulsatile	Centrifugal hydraulic	900 g	Ventricles
CARMAT[7]	Pulsatile	Electro-hydraulic	900 g	Ventricles
ReinHeart[8]	Pulsatile	Electromagnetic	940 g	Ventricles
OregonHeart[13]	Pulsatile	Electromagnetic	?	Ventricles
SoftTAH[9]	Pulsatile	Pneumatic	?	Ventricles
HybridHeart	Pulsatile	Pneumatic	≤900g	Ventricles

TECHNOLOGICAL REQUIREMENTS

Biocompatibility considerations

The HybridHeart is aiming to be a fully biocompatible device with a very low risk profile of thromboembolic events. If the foreseen hemocompatibility level is reached, during the operation of HybridHeart there will be no need for administering any anticoagulants such as coumarins, heparins or NOACs. This would significantly reduce the risks of any thromboembolic events compared to other TAHs: only a maintenance dose of aspirin will be required. In order to achieve this excellent hemocompatibility profile, the consortium aims to develop a tissue engineered inner lining and at the same time research the optimal fluidodynamic combination between valves and ventricular shape.

More specifically, for what concerns the ventricular shape, it will mimic as closely as possible the natural one, while for the valves, they will be provided by XELTIS and their dimensions should be in line with the ones typically used for TAH devices, i.e. SynCardia[4] range of 25-27 mm, HH range of 22-25 mm in diameter for both inlet and outlet.

Moreover, the inner lining of the HybridHeart will either be completely made of tissue engineered material, or a special coating that coupled with the soft robotics matrix made of polyurethanes/silicones will be able to repel all circulating cells and thus it will not induce any thrombus formation.

CONCLUSION

Final considerations

The HybridHeart project aims to design the first soft robotic and fully biocompatible total artificial heart: indeed, no present technology has been yet deemed reliable enough to become the optimal destination therapy for end-stage heart failure patients.

The development of an innovative type of total artificial heart, however, involves the definition of a high number of requirements, due to the extreme complexity and importance of the problem that it wants to solve. This document is summary of all the efforts made by the HybridHeart consortium. Indeed, thanks to the expertise and interdisciplinarity, characterizing all its members, it was possible to lay a strong basis for the design of this farsighted device. Although we are aware of all the challenges we are about to face, we still strongly believe that in the future the technology we are proudly developing could become the final solution to one of the most important causes of mortality worldwide.

REFERENCES

1. Altieri F, Watson J, Taylor KJJoba. Mechanical support for the failing heart. 1986;1(1):106-156.
2. Marieb EN, Hoehn KJHa, physiology. The cardiovascular system: blood vessels. 2004:703-720.
3. Sembulingam K, Sembulingam P. *Essentials of medical physiology*: JP Medical Ltd; 2012.
4. Slepian MJ, Alemu Y, Soares JS, Smith RG, Einav S, Bluestein DJJoB. The Syncardia™ total artificial heart: in vivo, in vitro, and computational modeling studies. 2013;46(2):266-275.
5. Dowling RD, Gray Jr LA, Etoch SW, et al. The AbioCor implantable replacement heart. 2003;75(6):S93-S99.
6. Jansen P, van Oeveren W, Capel A, Carpentier AJEJoC-TS. In vitro haemocompatibility of a novel bioprosthetic total artificial heart. 2012;41(6):e166-e172.
7. Carpentier A, Latrémouille C, Cholley B, et al. First clinical use of a bioprosthetic total artificial heart: report of two cases. 2015;386(10003):1556-1563.
8. Pelletier B, Spiliopoulos S, Finocchiaro T, et al. System overview of the fully implantable destination therapy—ReinHeart-total artificial heart. 2014;47(1):80-86.
9. Cohrs NH, Petrou A, Loepfe M, et al. A soft total artificial heart—first concept evaluation on a hybrid mock circulation. 2017;41(10):948-958.
10. Blomgren GEJJoTES. The development and future of lithium ion batteries. 2017;164(1):A5019-A5025.
11. Linden D. Linden's Handbook of batteries 4th edn. ed. by T. Reddy: McGraw-Hill Professional; 2010.
12. Wells D, Villa CR, Morales DLS. The 50/50 cc total artificial heart trial: extending the benefits of the total artificial heart to underserved populations. Paper presented at: Seminars in Thoracic and Cardiovascular Surgery: Pediatric Cardiac Surgery Annual2017.
13. Glynn J, Song H, Hull B, et al. The OregonHeart total artificial heart: design and performance on a mock circulatory loop. 2017;41(10):904-910.