Initial Pre-Clinical Studies (In-vivo)

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Studies Have Proven

- ART treatment in hypoxemic animal model, resulted in significant increase of oxygen saturation of 8%-10%
- A flow of 1 liter per minute, was sufficient to provide a saturation increase of 8-10%
- Pulmonary artery saturation, exhibiting ART oxygenation independent of oxygenation resulting from lung activity, increased by 26%
- ART exhibited a significant decrease of $PaCO_2$
- Blood pressure was unaffected

Pre-clinical Studies (In-vivo)

When: August 2020[1]

Tested: ART's ability to rebalance oxygen saturation levels within minutes

Where: LAHAV CRO in Israel[2]

Animal model: Swine model

ART system used for the studies: Lab unit constructed from lab components

25 hypoxemic events were induced

In 20 out of the 25 hypoxemic events induced, ART treatment[3] was provided with a blood flow rate of 1 liter per minute.

The results are presented here from these studies

Additional studies were conducted

- During 2019-2020, additional 15 pre-clinical studies were conducted as feasibility tests.
- On November 2021, an additional pre-clinical study was conducted in LAHAV CRO in Israel.

1. Research protocol was approved by the national ethics committee of animal experimentations.
2. LAHAV CRO https://lahavcro.com/
3. ART Treatment = extracorporeal blood oxygenation with one liter of blood

Method

In these initial pre-clinical studies (In-vivo) the goal was to assess the oxygenation effectiveness of ART system[1] in animal model.

Animal model

The swine species chosen for the current study is Large-White X Landrace. **This breed was chosen due to a well-known resemblance of the anatomy, cardiovascular and respiratory physiology, size scale and other characteristics to adult humans.**

Experiment setup

Two anesthetized mechanically ventilated swine, were cannulated in the right internal jugular vein via a double lumen cannula. The cannula conduits were connected to 3/8” diameter inlet & outlet tubes, allowing for blood transportation to and from the veno-venous ART device.

Hypoxemia induction

Intubated swine were ventilated with hypoxemic gas-mixture resulting in oxygen saturation level of ~80-85%. Hypoxemia was induced prior to each initiation of ART treatment

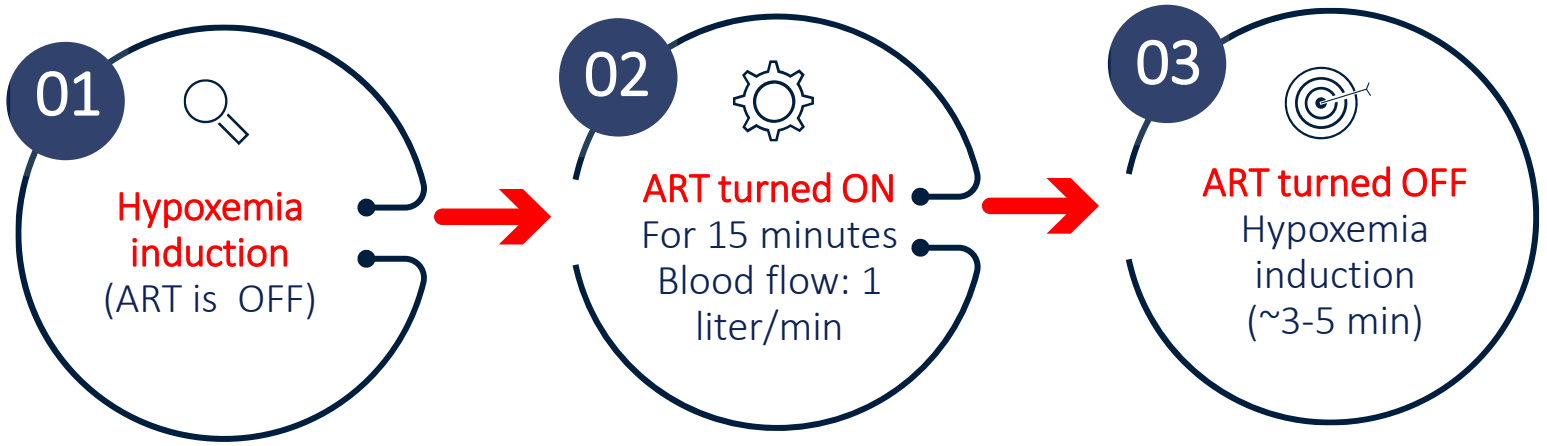
1. An extracorporeal respiratory support system composed of an oxygenator, a pump, a plug-and-play cartridge, sensors, and a control unit

Data Collected

Clinical and physiological parameters were collected throughout the test. Oxygenation was assessed by means of a non-invasive sensor (PPG-Sat), and blood gas measurements. Both arterial and venous blood were drawn and analyzed using the GEM 4000 Blood Gas Analyzer (Werfen, Barcelona, Spain). Blood pressure was assessed from pressure probes located in the femoral vein and carotid artery. An arterial sample (drawn from the carotid artery) and a venous sample (drawn from the femoral vein) were assessed for partial oxygen pressure (pO_2), oxygen-bound hemoglobin (O_2HGB), blood gas saturation, carbon dioxide partial pressure (pCO_2), bicarbonate levels (HCO_3), hemoglobin (HGB), hematocrit (HCT), pH, glucose, and electrolytes (sodium, potassium, chloride and ionized free calcium).

Study design

Blood oxygenation and CO2 removal at a flow rate of 1 litter/min were assessed in 20 consecutive observations, each repeated the following steps:

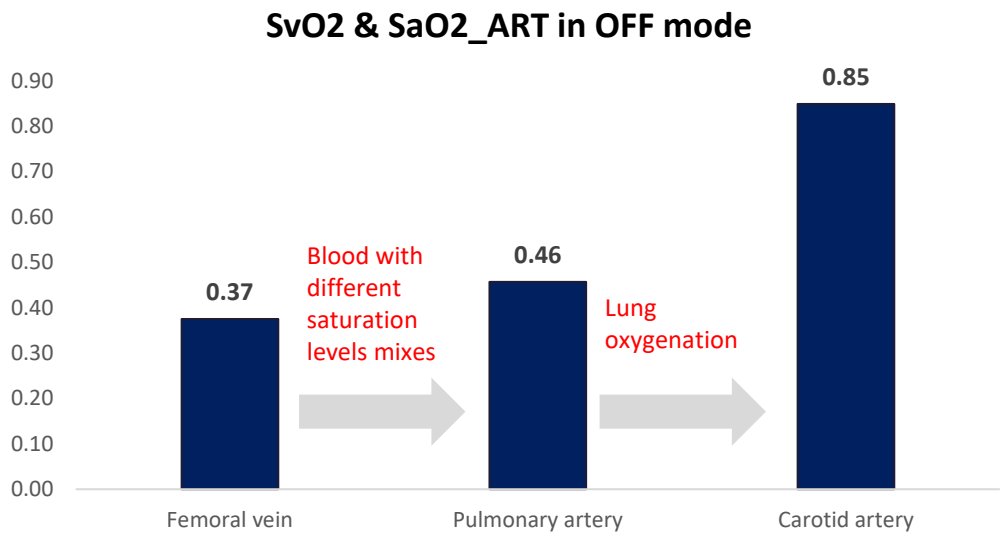


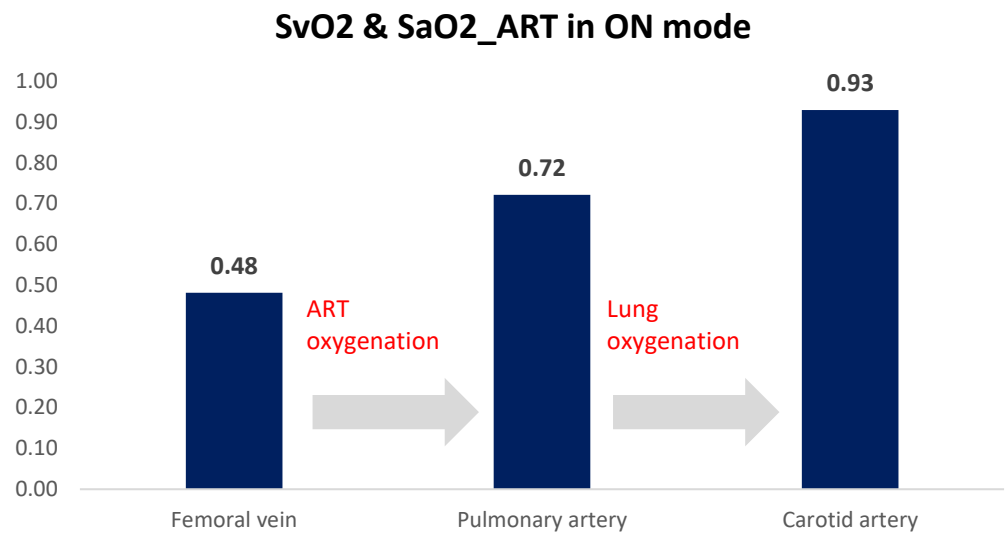
Blood samples are taken from the (1) femoral vein (2) pulmonary artery, and (3) carotid artery at baseline (prior to the activation of ART) and 15 minutes following the system's activation.

Study Results

ART Provides Significant Increase In Saturation

The saturation levels in the pulmonary artery increased on average by 26%, and in the carotid artery by about 8-10%



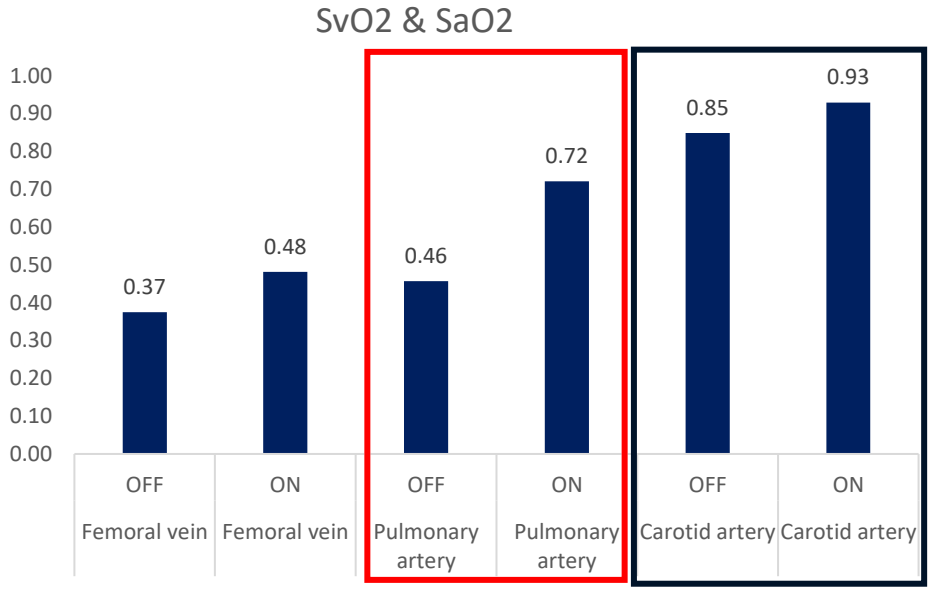


Parameter	Blood sample location	ART Status	ART Status	Difference	Std Error	t Ratio	Prob>|t|	Lower 95%	Upper 95%
SvO2 (%)	Femoral vein	OFF	ON	-0.106405	0.029932	-3.55	<0.005	-0.1694	-0.04341
SaO2 (%)	Pulmonary artery	OFF	ON	-0.264375	0.034515	-7.66	<.0001	-0.33689	-0.19186
SaO2 (%)	Carotid artery	OFF	ON	-0.080208	0.009376	-8.55	<.0001	-0.09991	-0.06051

ART's Contribution to Oxygen Saturation Should Be Reviewed Independently From the Lung Activity

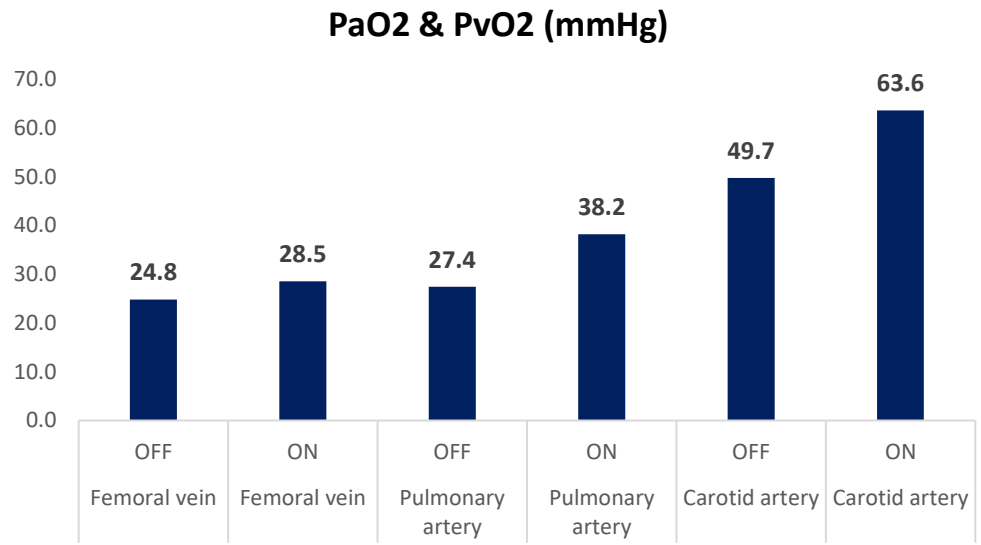
ART increased saturation by 26% in the Pulmonary Artery

The contribution of ART to saturation should be assessed via saturation measured in the Pulmonary artery; right after ART oxygenates 1 liter of blood and just before the patients' entire Cardiac Output further oxygenates via the lungs.



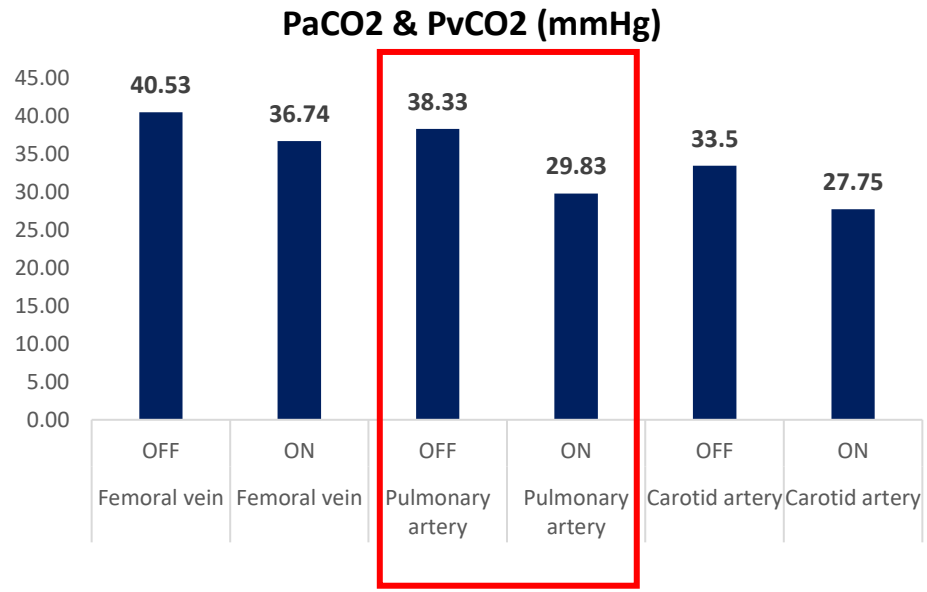
Disclaimer: The oxygenation capabilities of a patient/animal model lung will depend on the underlying pathophysiology, the level of severity and response to treatment.

ART Provides Significant Increase In PO2 Levels



Parameter	Blood sample location	ART Status	ART Status	Difference	Std Error	t Ratio	Prob>|t|	Lower 95%	Upper 95%
PO2 (mmHg)	Femoral vein	OFF	ON	-3.688546	1.316849	-2.8	0.0122	-6.46393	-0.91316
PO2 (mmHg)	Pulmonary artery	OFF	ON	-10.75	1.632462	-6.59	<.0001	-14.1797	-7.32033
PO2 (mmHg)	Carotid artery	OFF	ON	-13.833333	1.272559	-10.87	<.0001	-16.5069	-11.1598

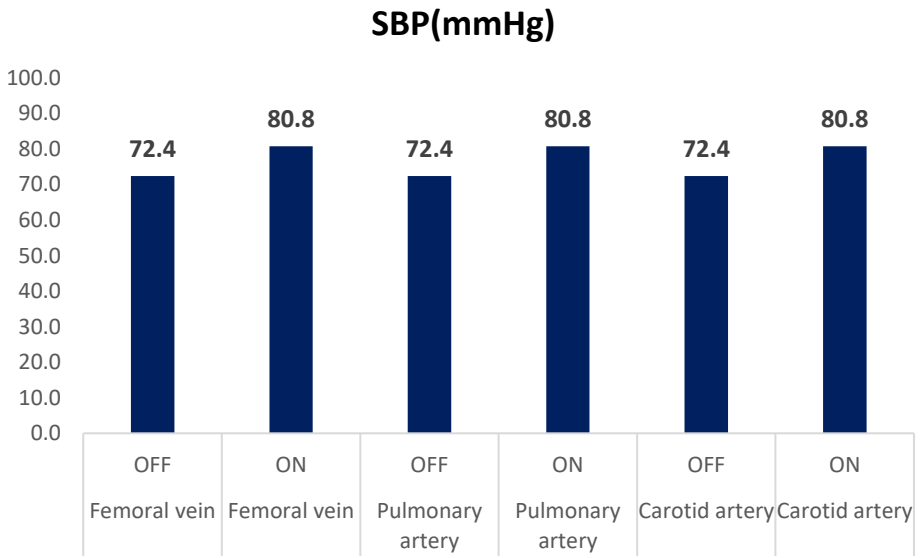
CO2 Removal Via ART Is Significant

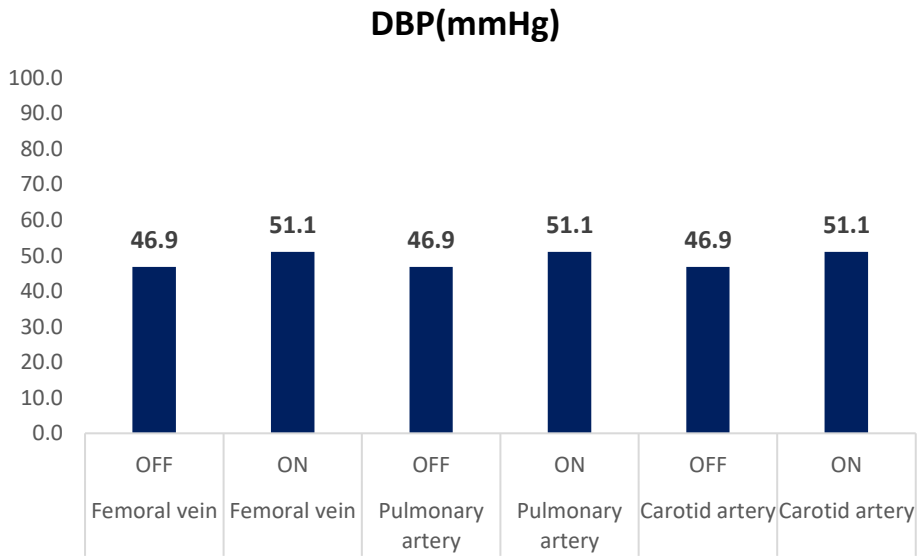


ART contribution to PCO2 decrease

Parameter	Blood sample location	ART Status	ART Status	Difference	Std Error	t Ratio	Prob>|t|	Lower 95%	Upper 95%
PCO2 (mmHg)	Femoral vein	OFF	ON	3.8	2.591466	1.46	0.1609	-1.64929	9.220551
PCO2 (mmHg)	Pulmonary artery	OFF	ON	8.5	1.707613	4.98	<.0001	4.91244	12.08756
PCO2 (mmHg)	Carotid artery	OFF	ON	5.8	0.699289	8.22	<.0001	4.28085	7.219151

Blood Pressure Was Unaffected





Parameter	Blood sample location	ART Status	- ART Status	Difference	Std Error	t Ratio	Prob>|t|	Lower 95%	Upper 95%
SBP (mmHg)	Femoral vein	OFF	ON	-8.45	1.762394	-4.8	0.0001	-12.1547	-4.74943
DBP (mmHg)	Femoral vein	OFF	ON	-4.19	1.172648	-3.57	0.0022	-6.65322	-1.72594
SBP (mmHg)	Pulmonary artery	OFF	ON	-8.45	1.762394	-4.8	0.0001	-12.1547	-4.74943
DBP (mmHg)	Pulmonary artery	OFF	ON	-4.19	1.172648	-3.57	0.0022	-6.65322	-1.72594
SBP (mmHg)	Carotid artery	OFF	ON	-8.45	1.762394	-4.8	0.0001	-12.1547	-4.74943
DBP (mmHg)	Carotid artery	OFF	ON	-4.19	1.172648	-3.57	0.0022	-6.65322	-1.72594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