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RESEARCH ARTICLE

Safety and performance of a novel implantable sensor in the inferior vena cava under acute and chronic intravascular volume modulation

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Aims

The management of congestion is one of the key treatment targets in heart failure. Assessing congestion is, however, difficult. The purpose of this study was to investigate the safety and dynamic response of a novel, passive, inferior vena cava (IVC) sensor in a chronic ovine model.

Methods and results

A total of 20 sheep divided into three groups were studied in acute and chronic *in vivo* settings. Group I and Group II included 14 sheep in total with 12 sheep receiving the sensor and two sheep receiving a control device (IVC filter). Group III included an additional six animals for studying responses to volume challenges via infusion of blood and saline solutions. Deployment was 100% successful with all devices implanted; performing as expected with no device-related complications and signals were received at all observations. At similar volume states no significant differences in IVC area normalized to absolute area range were measured ($55 \pm 17\%$ on day 0 and $62 \pm 12\%$ on day 120, $p = 0.51$). Chronically, the sensors were completely integrated with a thin, reendothelialized neointima with no loss of sensitivity to infused volume. Normalized IVC area changed significantly from $25 \pm 17\%$ to $43 \pm 11\%$ ($p = 0.007$) with 300 ml infused. In contrast, right atrial pressure required 1200 ml of infused volume prior to a statistically significant change from 3.1 ± 2.6 mmHg to 7.5 ± 2.0 mmHg ($p = 0.02$).

Conclusion

In conclusion, IVC area can be measured remotely in real-time using a safe, accurate, wireless, and chronic implantable sensor promising to detect congestion with higher sensitivity than filling pressures.

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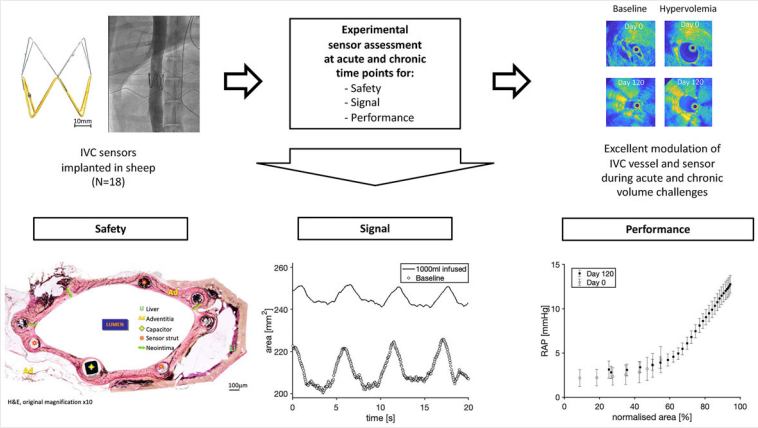
Graphical Abstract



A wireless inferior vena cava (IVC) sensor was implanted in sheep followed by experimental sensor assessment at acute and chronic time points including safety, signal, and sensor performance during manipulation of volume status. All sensors were safe and provided signal at all time points. The performance study (bottom right) showed that the sensors responded equally well to volume infusion (100 ml per data point) at acute and chronic observations, demonstrating the sensor's ability to detect volume accumulation consistently and reliably. Furthermore, IVC area changes were more sensitive than the corresponding changes in cardiac filling pressures, that is right atrial pressure (RAP) during manipulation of volume status.

Keywords Heart failure • Inferior vena cava • Right atrial pressure • Models • Animal • Chronic and acute response • Intravascular congestion

Introduction

Acute decompensated heart failure (ADHF) is characterized by excessive salt and water retention leading to congestion. Congestion is also the main target for therapy in patients hospitalized with ADHF. However, assessing and monitoring congestion poses significant challenges for effective disease management.[1–4] Indeed, insufficient detection and treatment of congestion contributes to the high rates of hospitalizations in patients with chronic disease.[5–7] Although remote monitoring of pulmonary artery pressure has been demonstrated to reduce heart failure (HF)-related hospitalization by up to 37%, the absolute rate of HF events remained high; death or HF-related hospitalization occurred in over 30% of the monitored patients at 1 year, reflecting significant residual risk of events.[8] Further, in the recent GUIDE-HF trial a remote pressure monitoring system implanted in patients with milder forms of HF did not result in a significant improvement in clinical outcomes in the full cohort analysis – likely to have been impacted by the effects of the COVID-19 pandemic.[9] Given the limitations of the current standard of care, it remains unclear how to optimally detect and manage congestion in ambulatory patients with a bid to reducing hospitalization, morbidity and mortality.

Absolute inferior vena cava (IVC) diameter and the degree of collapsibility with inspiration (collapsibility index [CI]) have been established as tools to assess volume status and fluid responsiveness in multiple clinical settings.[10] IVC dilatation has been shown to be associated with an increased risk of early readmission and short-term mortality in patients hospitalized for ADHF,[11] while in patients with chronic HF, increasing IVC diameter has been demonstrated to correlate with adverse outcomes.[12] However, ultrasound imaging of the IVC is challenging with considerable intra-operator variability and often limited imaging windows due to body habitus. Compared to ultrasound of other cardiac structures, IVC size (<2.5 cm diameter) and depth within the abdomen (>10 cm away from transducer) pose major technical challenges.[13] In one study, sufficient image quality of the IVC was only obtained in 57% of patients when scanned by trained nurse operators.[14] It is therefore hypothesized that the use of an implanted device that monitors IVC geometry (size and collapsibility) in real time may allow detection of clinically significant increases of intravascular volume with a higher sensitivity than filling pressures. This would facilitate earlier therapeutic interventions aimed at counteracting hypervolaemia and may as a result help reduce HF hospitalization rates and improve exercise tolerance and quality of life. In a first pre-clinical study with the FIRE1 System (Foundry Innovation & Research 1 Ltd., FIRE1, Dublin, Ireland), it was shown that IVC area is a more sensitive measure than filling pressure when intravascular volume and tone were modulated acutely.[15]

The aim of this study was to demonstrate the safety and performance of this new system, as well as to define its dynamic

response to intravascular volume modulation during the acute and chronic stages following implantation. Particular attention was paid to device endothelialization and its possible effects on vessel/sensor compliance. It is hypothesized that the IVC sensor would demonstrate complete endothelialization into the IVC intima and that such neointimal integration during chronic healing would have no effect on sensor accuracy or its response to infused volume.

Methods

The purpose of this study was to investigate the safety and dynamic response of a novel, passive, IVC sensor with remote monitoring capability in a chronic ovine model.

The FIRE1 system

The FIRE1 system includes an implanted sensor and an external electronic system utilizing a radiofrequency antenna embedded in an externally worn belt (*Figure 1A*) connected to a signal processing unit that communicates with a cloud-based web application to store and visualize the recorded IVC area data. The implantable sensor (*Figure 1B*) is a crown-shaped implant that is deployed in the IVC between the hepatic and renal veins. The passive sensor contains no battery and is constructed using nitinol components providing a low radial force, barbs to prevent migration, and gold wire connected to a capacitor forming a resonant circuit. Communication between sensor and externally worn belt is wireless (*Figure 1C*). As the sensor flexes during the respiratory and cardiac cycles, the inductance of the resonant circuit changes and thus, the resonant frequency changes (*Figure 1D*). Two example spectra are shown for a larger and a smaller IVC in *Figure 1E*. Upon analysis, the results provide a measurement of the internal cross-sectional area of the IVC. An example area trace exhibiting slow modulation with respiration and fast modulation with cardiac heartbeat is shown in *Figure 1F*. Data summarizing *ex vivo* and acute and chronic *in vivo* testing of the accuracy with which this system measures cross-sectional area is provided in online supplementary materials and *Figure Appendix S1*. In brief, the system was shown to be accurate in reference to area measured using intravascular ultrasound (IVUS) to $13 \pm 41\ mm^2$ (mean ± 95% confidence interval).

In vivo study

An *in vivo* study was performed in a total of 20 sheep divided into three groups that were studied in acute and chronic settings. Experiments were conducted at Institute Mutualiste Montsouris (IMM Recherche, Institut Mutualiste Montsouris-42, Paris, France) and the experimental protocol was approved by the IMM Recherche Institutional Study Animal Care and Use Committee before study initiation. All animals received humane care in compliance with the Guide for the Care and Use of Laboratory Animals. Animals were pre-medicated using midazolam and morphine. Anaesthesia was induced using sodium thiopental and was maintained using isoflurane delivered through endotracheal intubation and mechanical ventilation. Anticoagulation treatment consisted of enoxaparin subcutaneously twice a day until day 30 post-implantation and aspirin once a day until sacrifice. This anticoagulation treatment regimen simulated the 1-month dual anti-platelet therapy to be administered to patients in future clinical trials. Venous and arterial access were obtained by vascular cut down or percutaneous approach via catheters placed in the iliac vein, iliac artery, carotid artery and jugular vein. IVC area was measured using the FIRE1 implantable sensor which was placed in the IVC using fluoroscopy and IVUS via femoral venous access using an introducer sheath (Cook Medical, Bloomington, IN, USA).

Sensor safety and performance (Group I and II)

A total of 14 sheep were studied, seven of which were survived for 90 days (Group I) and seven which were survived for 180 days (Group II) (see study design in online supplementary *Figure S2*). In each of these two groups, six animals received a FIRE1 implant and one animal received an implant of a control device (Cordis Trapease® Permanent Vena Cava filter [466-P306B]). Procedural success and FIRE1 sensor signal were assessed at the conclusion of the implant procedure (designated study day 0). Signal, sensor fracture, vessel perforation and sensor migration were also assessed in all study animals at the intermediate follow-up assessments at days 30 and 90 via X-ray, angiography (full power contrast injection) and use of the FIRE1 external system. The long-term performance of the FIRE1 system was assessed at day 180 angiographically, with IVUS (iLabTM system with Ultra-ICE Plus catheter, Boston Scientific, MA, USA) and with the FIRE1 system signal recording. Sensor signal was also monitored at day 180 to demonstrate whether the sensor signal was affected by incorporation into the vessel wall during long-term follow-up. At necropsy, the IVC was excised *in situ* and internal videoscopy was performed along with high resolution X-ray (Faxitron®) analysis for fractures and mineralization evaluation. Local and systemic toxicity as per international engineering standards (ISO10993-6 and ISO10993-11, respectively), were assessed during follow-up (clinical observations and clinical pathology) and at necropsy through macroscopic evaluation of organs and histopathology. Histology was performed on all Group I and Group II animals. Standard samples from the organs and from macroscopic findings were embedded in paraffin following standard processing methods.

Volume challenge (Group III)

This protocol included six animals, each implanted with a FIRE1 sensor which underwent repeated volume challenges at day 0, before and after deployment, as well as on days 60 and 120. Pressures were monitored by Millar Mikro-Cath™ pressure catheters (Millar, 825-0101, Houston, TX, USA) in the right atrium and recorded using Powerlab (AD Instruments, Colorado Springs, CO, USA). Each animal underwent initial venesection to obtain an initial starting right atrial pressure (RAP) of ~2 mmHg. All extracted blood was stored in standard citrate phosphate dextrose adenine blood collection bags to ensure the blood remained stable for re-infusion. After an approximate 30 min period of equilibration allowing plasma refill, the extracted blood was injected in boluses of 50 ml with 2 min of equilibration after each bolus. Once the extracted blood was reinfused, volume infusion was continued using saline solution until a target RAP of 15 mmHg or clinical instability (e.g. progressive hypoxia) occurred. IVC area measured by the implanted sensor and RAP were monitored throughout the infusion period.

Statistical analysis

Continuous variables were summarized as mean ± standard deviation according to the observed distribution.

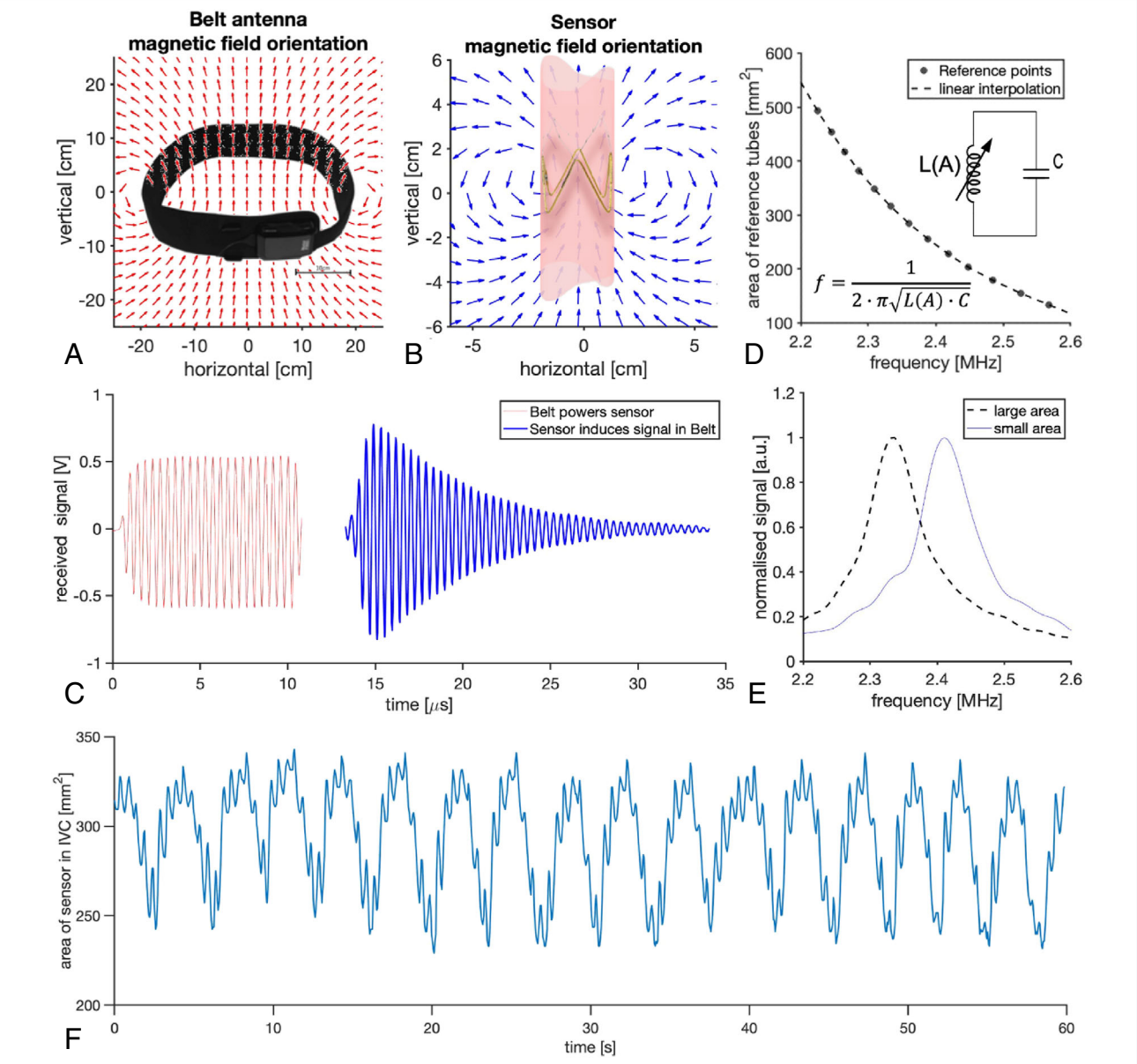


Figure 1 The inferior vena cava (IVC) area recording sensor and system used for this study comprising of (*A*) an electronic system incorporated in belt antenna, and (*B*) an implantable sensor. (*C*) General concept of magnetic field coupling utilized for belt antenna to charge sensor via a brief pulse of 10 μs length (red trace) and for sensor to couple into belt antenna during receive period resulting in free induction decay recording (blue trace) – encoding IVC area information in the signal's resonance features. (*D*) Sensor concept of the electromagnetic resonance based sensor, model linking the sensor's resonance frequency and the actual sensor area as measured in tubes of known cross-sectional area. (*E*) Two example frequency spectra of a large and a small IVC. (*F*) trace composed of 1100 area values as a function of time in seconds – the area trace from which ultimately area max, mean and min as well as collapsibility index are extracted for further trending purposes.

Area normalization for volume challenge (Group III)

For the volume challenge experiments, changes in IVC area and RAP as a function of infused volume were compared. Given that there was significant heterogeneity in the size of the IVC between animals, normalization of the IVC area was necessary and was adopted from most recent report.[15] For this comparison, the area range ($A_{total,range}$) was first determined for each animal (considering all area measurements on day 0 and day 120 [$A_{total,range}$] was computed as the difference of the observed maximum area [$A_{total,max}$], minus the observed minimum area [$A_{total,min}$]). For each trace the mean area (A_{mean}) was computed as (A_{min} + A_{max})/2. Then, the normalized mean area ($A_{mean,norm}$) from a trace was calculated from A_{mean} as a percentage of the area range as follows: (A_{mean} − $A_{total,min}$)/$A_{total,\ range}$ × 100%. Mean RAP and normalized area traces of 15 s lengths were averaged at each

volume level for each of the six animals. Mean and standard error of the mean values were computed from the six animals and were reported for every 100 ml of infusion volume.

Testing sensitivity of normalized area and right atrial pressure to infused volume (Group III)

It was hypothesized that changes of normalized area were more sensitive to changes in volume status than RAP. Normalized areas obtained at each level of infusion were compared to the starting, control condition (i.e. at 0 ml infused volume). Data were analysed with a repeated measures ANOVA with post hoc Dunnett's tests to correct for multiple comparisons to the control condition. A p-value <0.05 was considered statistically significant. Processing and analysis of traces was completed using MATLAB (Mathworks 2021a, Natick, MA, USA).

Results

Sensor safety and performance (Group I and II)

Sensor deployment and follow-up

All implantation procedures were successfully executed, with the sensors deployed in the target landing zone and in stable position at the end of the procedure (online supplementary material, deployment video [*Video S1*]). Post implantation, IVUS was repeated and sensor lumen apposition was deemed excellent in all cases. Due to the elliptical nature of the IVC, the mean IVC diameter was determined from the average of the major and minor diameters at its maximal size using IVUS. Mean IVC diameter for study I and II was 17.7 mm (range 15.1–24.1 mm, $n = 14$) and 13.4 mm (range 10.2–16.6 mm, $n = 6$) for study III.

Freedom from sensor complications

No complications were observed in any of the animals. There was no migration, fracture, IVC perforation, vessel damage, caval thrombosis or caval occlusion noted at implant or at any follow-up evaluations. No evidence of local or systemic toxicity and thrombogenicity related to the sensors was observed as assessed by gross necropsy, macroscopic evaluation, histopathology assessment of IVC and major organs, and regular clinical observations throughout the study. The sensors were completely integrated with a thin, endothelialized neointima (*Figure 2A–C*). No degradation of signal performance was noted over the course of the study. Examples for signal-to-noise ratio (SNR) as the performance endpoint for one exemplary sheep at day 0, 30, and 90 are shown in online

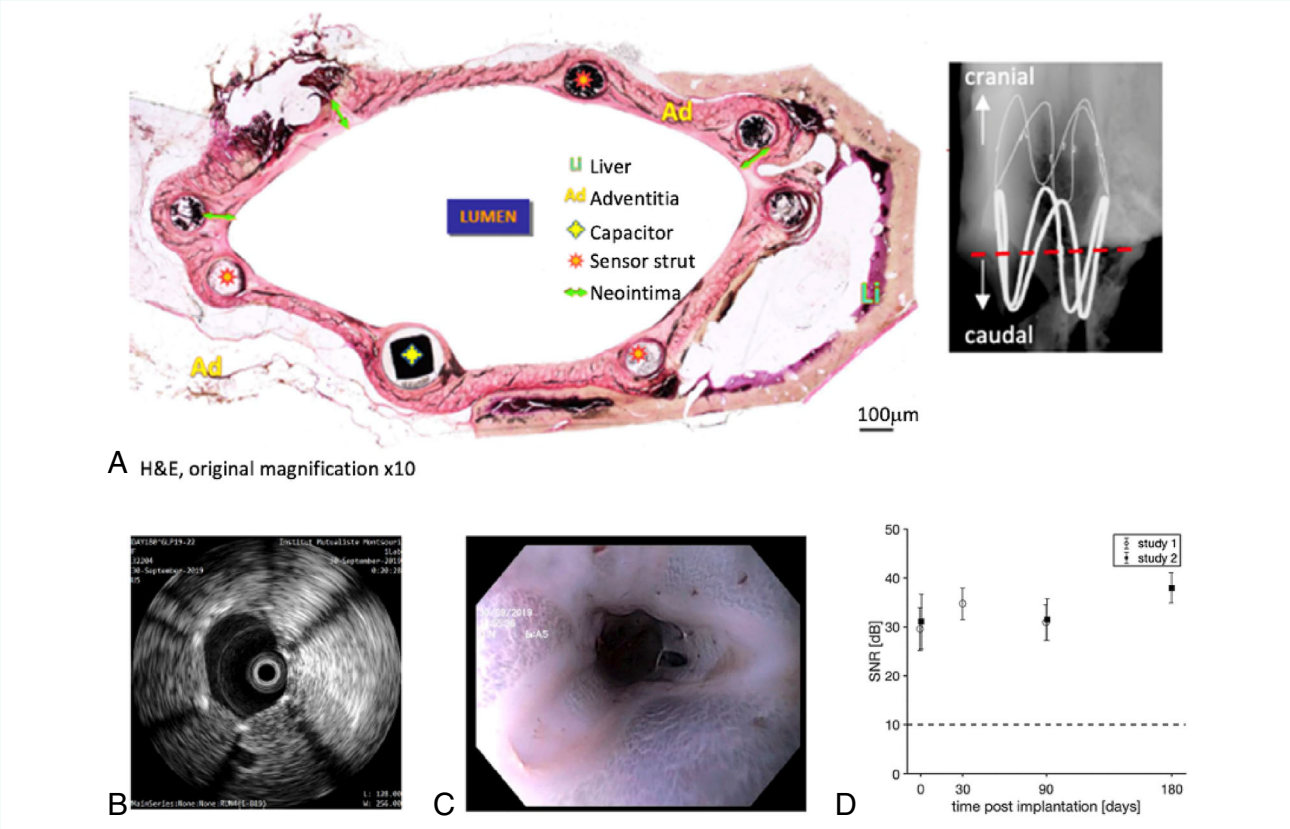


Figure 2 Sensor displayed excellent inferior vena cava (IVC) apposition, integration and coverage at day 180 after implantation as evidenced by (*A*) hematoxylin and eosin (H&E) stain using histology with inset faxitron/X-ray image of explanted sensor, (*B*) intravascular ultrasound, and (*C*) videoscopy. Signal was well above signal-to-noise ratio (SNR) threshold at 10 dB (dashed line) and did not significantly vary in between observation days as evidenced by (*D*) SNR measured at various time points after implantation.

supplementary *Figure S3*. The mean and standard deviation of SNR as a function of time after implantation is presented in *Figure 2D*.

Volume challenge (Group III)

Inferior vena cava responses to volume challenges in the acute and chronic settings were measured in all six animals included in this study. Implant of the IVC sensor within the pre-specified landing zone was successful in all animals without complication. No migrations, fractures or thrombus were observed. The volume experiment was completed in all six animals at all four observation points (before and after deployment on days 0, and again at days 60 and 120). *Figure 3* shows IVUS images of the landing zone before deployment and 120 days after implantation, both at baseline infusion point during hypovolaemia and at the maximum infusion point during hypervolaemia. At baseline after fluid removal, the IVC presented characteristically an elliptical shape. This collapsed shape was observed acutely before deployment as well as chronically with sensor on day 120. Furthermore, at 120 days all sensors were well incorporated with neointima without struts inside the lumen, yet retaining the ability of the sensors to follow physiological IVC geometric changes from elliptical to circular with volume infusion and throughout the respiratory cycle. Comparing the area in the hypervolaemic state with maximum size achieved before deployment and that observed after 120 days confirmed excellent qualitative concordance.

Figure 4 shows pressure and sensor area traces as a function of infused volume as a function of bolus injection time at day 120 from a representative Group III animal. In the low-pressure range below 6 mmHg and for infusion volumes below 1000 ml, large changes of IVC area occurred with relatively small changes of RAP. Once RAP reached ~6 mmHg small increases of volume infusion resulted in noticeable increases of pressure as expected. Collapsibility index decreased as volume infusion increased while there was relatively little change in the amplitude of the RAP tracing.

Figure 5 shows the averaged results from the six animals studied on day 0 and day 120. There were no observed significant differences for mean normalized area between day 0 and day 120 at similar volume states of 700 ml volume infused (55 ± 17% on day 0 vs. 62 ± 12% on day 120, $p = 0.51$) confirming that neointima formation did not significantly affect the dynamic behaviour of the IVC with the chronically implanted sensor.

Comparing observations at various infusion points at day 0 showed that, compared to baseline, normalized area increased by a statistically significant amount after 200 ml infusion: from 9 ± 6% at 0 ml infused to 28 ± 7% at 200 ml infused ($p = 0.03$). In contrast, RAP did not increase significantly despite infusion of 700 ml (maximum infusion volume on day 0): from 2.2 ± 2.5 mmHg at baseline to 4.2 ± 4 mmHg with 700 ml infused ($p = 0.77$). The greater sensitivity of normalized area to volume infusions compared to RAP was confirmed at day 120: normalized area increased from 25 ± 17% at baseline to 43 ± 11% with 300 ml infused ($p = 0.007$) while there was no significant change in RAP (from 3.1 ± 2.6 mmHg at baseline to 3.4 ± 1.6 mmHg at 300 ml infused, $p = 1.0$). A large infusion of volume was required on day 120 to achieve significant change in RAP, increasing from

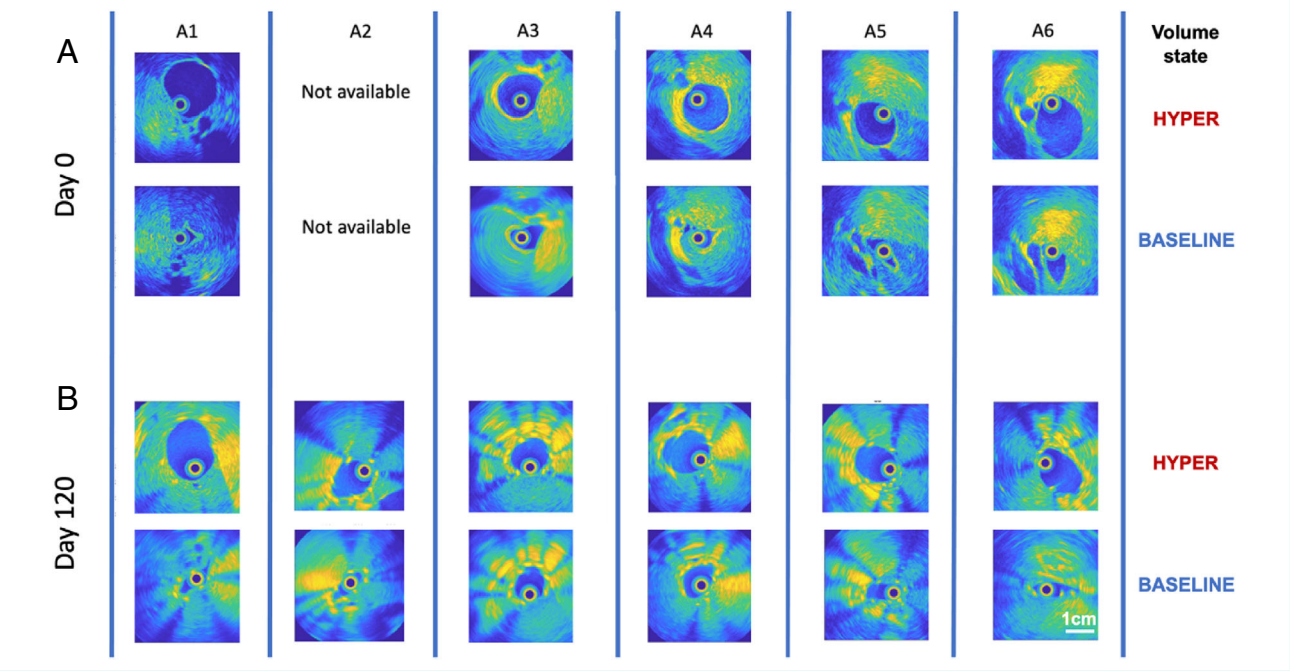


Figure 3 Intravascular ultrasound data showing native vessel before deployment in landing zone of sensor on day 0 (*A*) and after deployment during chronic day 120 observation (*B*) at the extreme intravascular volume status of maximally removed volume (Baseline) and at maximally filled volume (Hyper). Note excellent qualitative modulation with infused volume with and without sensor.

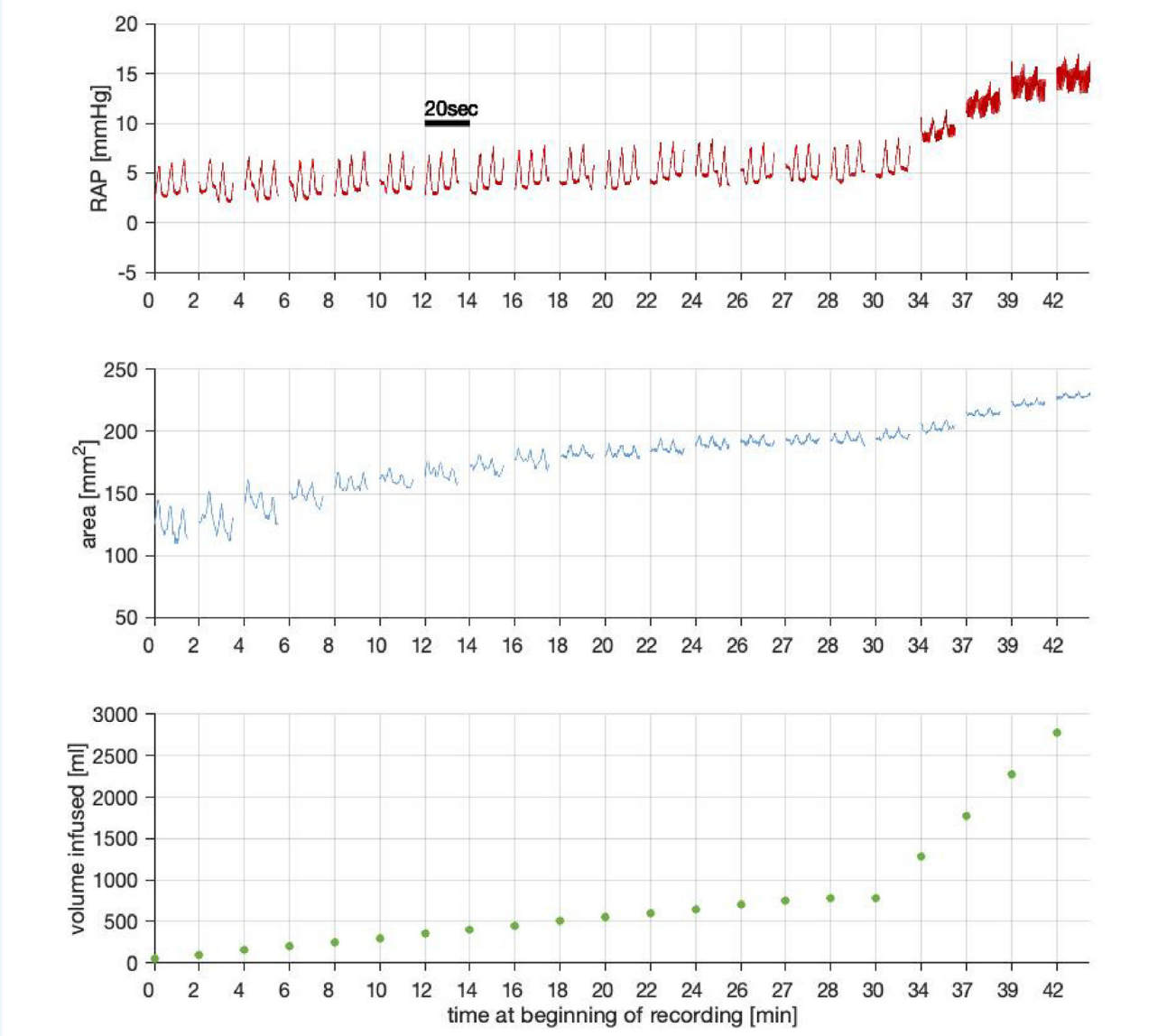


Figure 4 Trace data of right atrial pressure (RAP), area, and volume infused as a function of infusion time for one animal (animal 5) at chronic day 120. Collapsibility index reduced and area increased visibly with only 300 ml infused (at 10 min) with little increase in RAP.

3.1 ± 2.6 mmHg at baseline to 7.5 ± 2.0 mmHg at 1200 ml infused ($p = 0.02$). At 1200 ml infusion, normalized area increased from 25 ± 17% at baseline to 75 ± 7% ($p < 0.0001$). Note that the averaged RAP and normalized area data followed comparable trajectories when day 0 was compared to day 120.

Figure 6 further shows RAP as a function of normalized IVC area for the group averaged results, providing an index of IVC compliance. As expected, RAP varied relatively little in the range from 0 mmHg up to 6 mmHg while IVC normalized area ranged from 0% to 70% of its maximum possible size. The compliance, computed as a change of normalized area per change of pressure, averaged 12%/mmHg in the low-to-normal pressure range of 0 to 6 mmHg. Compliance decreased to 4%/mmHg for pressures above 6 mmHg.

Discussion

This study has demonstrated the safety and performance of the novel implantable remote monitoring device, that is, the FIRE1 sensor. The primary observations of this study were: (i) the FIRE1 sensor is a passive device which has shown to provide an accurate and precise measurement of cross-sectional area of the IVC over several months of follow-up; (ii) this sensor can be reliably and safely deployed in the IVC providing real-time information of IVC size during provocative manoeuvres in acute and chronic settings; (iii) increases in IVC area have been shown to be significantly more sensitive to volume loading than RAP, suggesting that intravascular volume expansion may be detected at an earlier stage of fluid accumulation using this approach.

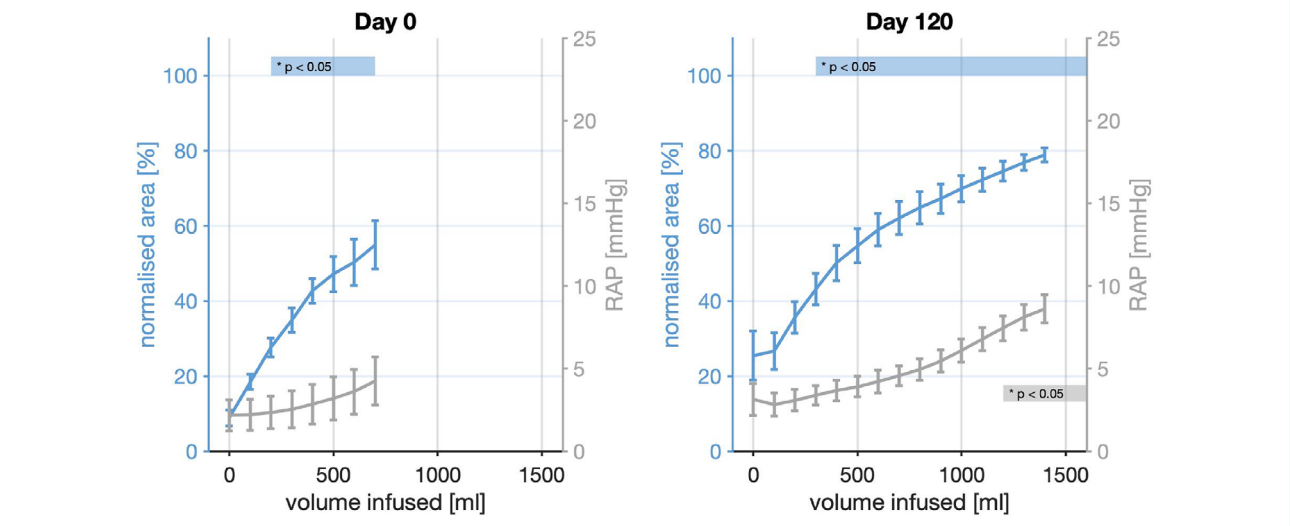


Figure 5 Day 0 (left) and day 120 (right) showing mean right atrial pressure (RAP) and normalized mean area of the inferior vena cava as a function of infused volume and averaged across six animals per data point. Error bars indicate standard error of the mean. Faint bar above in blue for normalized area of the inferior vena cava and in grey for RAP start at infusion level that was returned as significantly different ($p < 0.05$, repeated measures ANOVA with post hoc Dunnett's test) compared to measurements taken at 0 ml. Fluid infusion was stopped after 700 ml on day 0 to ensure survival and recovery of the chronic animals.

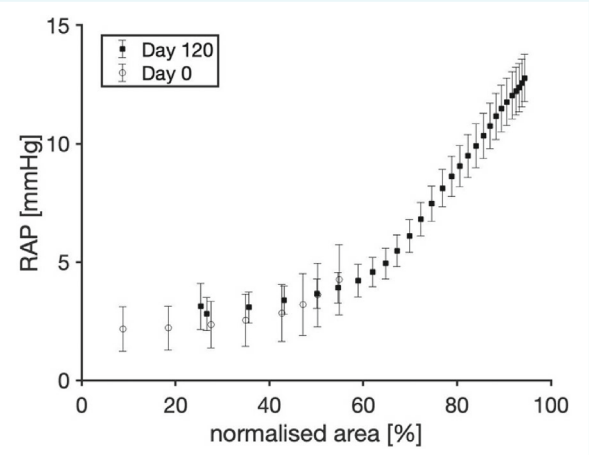


Figure 6 Mean right atrial pressure (RAP) as a function of mean normalized area graph for six sheep showing day 0 (open circles) and day 120 (filled squares) as fluid was infused from baseline shown here in steps of 100 ml between consecutive samples shown. Note the strong overlap of the two curves for comparable volumes. Further note the expected non-linear compliance curve with large changes of inferior vena cava area in low pressure zones (up to 6 mmHg) and more connected changes in RAP and inferior vena cava area thereafter. Error bars indicate standard error of the mean.

This may have significant clinical implications enabling the earlier detection of hypervolaemia in comparison to pressure sensors to facilitate early clinical action and beneficial clinical impact on the trajectory of HF patients; and (iv) implantation of the sensor within the IVC and its integration through endothelialization has been demonstrated to have had no detrimental impact on the long-term sensor performance in response to fluid accumulation. The sensors responded equally well to volume infusion at acute and chronic observations, demonstrating the sensor's ability to detect volume accumulation consistently and reliably (*Graphical Abstract*).

The finding that IVC area was more sensitive in detecting volume changes than pressure-based metrics was expected based on both prior studies using transthoracic ultrasound[16] and established physiologic principles.[17] The venous system is comprised of the most compliant vessels in the body (~30 times that of the arteries) and >70% of total blood volume resides in the venous compartment.[18,19] This large compliance and capacitance permits large changes in blood volume to be accommodated by large changes in vessel diameter with comparatively small changes in intravascular pressure. Furthermore, the venous system regulates preload via changes of its vascular compliance.[20] Pressure sensors only capture one variable that can link to high volume, yet filling pressure can also be elevated in cases with increased compliance and normal volume. In line with this physiology, filling pressures such as central venous pressure and pulmonary capillary wedge pressure have repeatedly demonstrated limited correlation with measures of volume status such as circulating blood volume and haemodynamic response to fluid challenge.[19,21–30] Additionally, the current findings are consistent with a recent study showing greater sensitivity of area measurements compared to pressure measurements in acute tests in which volume and vascular tone were manipulated.[15]

The total blood volume of the sheep used in this experiment is estimated to be approximately 4 L. Thus, infusing 300 ml of

blood represents a meaningful relative expansion of blood volume. However, this only translated into ~0.5 mmHg change in RAP when starting from a normal intravascular volume. Thus, when a patient with HF is adequately decongested, relatively large increases in intravascular volume may occur prior to increases in filling pressure.

The clinical implications of the current study are that chronic monitoring of an IVC area sensor may provide independent, incremental and/or additive information to pressure-based sensors. This may facilitate earlier intervention in HF patients before signs and symptoms arise or pressure-based monitoring indicate a significant change. Early intervention based on remote monitoring has been clearly demonstrated to reliably detect HF decompensation up to 30 days prior to an acute event. Volume-based area changes using the FIRE1 system may lead to significantly earlier detection in comparison to current pressure/device-based systems. These observations justify testing of chronic IVC remote monitoring in HF patients. Accordingly, the first in human clinical investigation of the FIRE1 device/system is ongoing (FUTURE-HF, NCT04203576) and will evaluate the feasibility and safety of implanting the FIRE1 sensor in stable HF patients.

Several limitations of the present study should be noted. The present investigations were designed to provide proof of concept that the IVC area reproducibly responds to volume challenges in acute and chronic conditions. They were conducted using healthy sheep with experimental manipulation of intravascular volume. In healthy models, higher preload is generally accompanied with higher cardiac output, and possibly less effect on pressure as compared to an animal model of HF. As such, findings of this study cannot be directly extrapolated to humans and particularly humans with HF. The volume loading experiment was designed to evaluate the pressure–IVC relationships starting at a low normal RAP to an elevated RAP, and the reported observations apply within this construct. However, given the non-linearity of the IVC pressure–area relationship and the effect of mechanical ventilation and anaesthesia on filling pressures, the absolute volume status of the animal was unknown and likely varied somewhat between animals. Furthermore, RAP values did not exceed 20 mmHg. Therefore, these findings should be regarded as hypothesis generating and additional research in chronic HF patients will be required to truly understand the potential of chronic IVC monitoring in the setting of human HF.

In conclusion, the present studies show that a wireless, passive radiofrequency-based sensor can be safely deployed in the IVC, allowing for remote assessment of IVC area in real time chronically. The IVC area was more sensitive to experimental volume infusion (acutely and chronically) compared with changes in RAP, with greater dynamic changes in the operating range of normal-to-moderately high venous pressures. These data suggest that chronic remote home monitoring using IVC-implanted devices may represent a valuable strategy to improve clinical management of patients with chronic HF.

Supplementary Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Acknowledgement

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Conflict of interest: DK reports Speaker fees for Abbott, Boehringer Ingelheim, and Astra Zeneca. JMT reports grants and/or personal fees from 3ive labs, Bayer, Boehringer Ingelheim, Bristol Myers Squibb, Astra Zeneca, Novartis, Cardionomic, MagentaMed, Reprieve inc., FIRE1, W.L. Gore, Sanofi, Sequana Medical, Otsuka, Abbott, Merck, Windtree Therapeutics, Lexicon pharmaceuticals, Precardia, Relypsa, Regeneron, BD, Edwards Lifesciences, and Lilly. MF, PG, and SM declare to serve as consultants for Fire 1. SS, FW, and FS have patents "Wireless Resonant Circuit And Variable Inductance Vascular Monitoring Implants And Anchoring Structures Therefore" US2021/0196199A1 and "Wireless Vascular Monitoring Implants" US10806352B2 both issued to FIRE1. All other authors have nothing to disclose.

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