cal activation of antimiRs could overcome this obstacle. To that end, we were able to synthesize light-inducible antimiRs by modifying oligonucleotides with photolabile protecting groups, so called "cages". We demonstrated that light-induced activation of caged antimiR-92a significantly improved angiogenic sprouting in vitro, consistent with previous studies in which conventional antimiRs were used. In further studies we were able to extend the use of caged antimiRs to an in vivo setting. Intradermal injection of caged antimiR-92a with subsequent light irradiation in murine skin led to a marked down-regulation of miR-92a expression that was as efficient as non-caged antimiR-92a application (caged antimiR-92a with light activation: –98±1%, $p<0.003$; antimiR-92a: –99±0.1%, $p<0.008$), while treatment with caged antimiR-92a without light activation had no effect (caged antimiR-92a: +20±17%, p=0.5). However, in contrast to conventional constitutively active antimiR-92a, the local activation of caged antimiR-92a did not inhibit the expression of miR-92a for example in liver tissue (caged antimiR-92a with light activation: +37±31%, antimiR-92a: –40±14%). Since quality and rapidity of tissue repair is dependent on the angiogenic response, wound healing is a suitable model to study the therapeutic potential of the pro-angiogenic antimiR-92a. Indeed, we were able to show, that administration of caged antimiR-92a led to improved tissue repair in healing impaired db/db mice after light activation. Caged antimiR-92a treated wounds reveal an accelerated healing kinetics (caged antimiR-92a with light induction: –30±13% wound size 11 days post injury, $p<0.05$), accompanied by a dense and cell-rich granulation tissue in comparison to non-irradiated antimiR-92a (caged antimiR-92a with light induction: +71±36%, $p<0.01$). Mechanistically, we were able to show that improved wound healing upon caged antimiR-92a treatment was based on increased capillary formation (caged antimiR-92a with light induction: +74±28%, $p<0.05$) and a significant derepression of the miR-92a target Sirt1 in comparison to controls (caged antimiR-92a with light induction: +56±14%, $p<0.01$). In conclusion, these data provide first in vivo evidence and proof-of-concept to demonstrate the feasibility and efficiency of light-induced activation of antimiRs. Local activation of antimiRs allows for a tissue-specific targeting of antimiRs reducing putative adverse effects of antimiRs in other tissues. This strategy may be used for therapeutic targeting of miRs in cardiac or vascular disease.

1889 | BENCH
The torpedo-pacemaker - towards blood flow driven lead- and batteryless right ventricular outflow tract pacing

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Background and introduction: Leadless pacemakers (PM) have been introduced recently. They overcome the need for the failure-prone pacing leads and therefore confer an advantage over conventional PMs. However, contemporary leadless PMs are powered by batteries offering only a limited energy storage capacity. When the battery approaches its end of life, the device has to be replaced (or another device has to be implanted if the leadless PM cannot be explanted). This Achilles' heel is accentuated by the limited volume in the right ventricle restricting the battery size.
Purpose: To overcome this limitation, a lead- and batteryless PM is desirable. We investigated the feasibility of energy harvesting by a blood flow driven generator in the right ventricular outflow tract (RVOT). This approach would allow building lead- and batteryless PMs for catheter-based implantation.
Methods: We developed a torpedo-like pacemaker generator for implantation in the RVOT. The device (diameter 6.2 mm, weight 3.6 g) features four self-expanding nitinol-struts for a centred alignment in the RVOT (figure). The blood flow drives a propeller which actuates a micro generator (MG 4.0, Netherlands). The micro generator converts the propeller rotation into electrical energy. The 3D printed propeller (outer diameter 10.2 mm) was designed for physiological flow conditions in the RVOT. To transfer the mechanical power while ensuring impermeability of the device, we built a magnetic coupling mechanism. This allows a permanent through-flow of blood which is aimed to reduce blood trauma (and the associated risk of thrombosis).
The prototype was tested on a flow bench mimicking hemodynamic conditions in the RVOT. Energy output of the generator was measured at a heart rate of 60 beats per minute.
Results: For a normal cardiac output of 4.6 l/min (stroke volume 77 ml), the generator delivered a mean power of 32.5±9.9 μW (the typical power consumption of modern leadless PMs is in the range of 5 μW). During systole, the turbine propeller rotates for 0.23±0.04 seconds and accelerates up to 2868±368 rotations per minute. The turbine generator increased the peak gradient in the RVOT by only 4 mmHg.

Blood flow driven turbine generator

Conclusion: Blood flow in the RVOT provides sufficient energy to power a pacemaker, enabling lead- and batteryless RVOT pacing.
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YOUNG INVESTIGATORS AWARDS SESSION: CLINICAL SCIENCE

1890 | BEDSIDE
Transcatheter aortic heart valve thrombosis: incidence and predisposing factors

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Background: Data on the incidence and predisposing factors of transcatheter heart valve (THV) thrombosis are sparse. Moreover, conventional post-transcatheter aortic valve replacement (TAVR) echocardiographic follow-up has proved inferior for the detection of THV thrombosis when compared to contrast-enhanced multidetector CT (MDCT). We sought to determine the incidence and potential predictors of THV thrombosis determined by MDCT.
Methods: Of 460 consecutive patients undergoing TAVR, 405 (Edwards Sapien XT, n=173; Edwards Sapien 3, n=232) underwent MDCT and echocardiographic follow-up 1–3 months post-TAVR. MDCT scans were evaluated for hypo-attenuated leaflet thickening indicating THV thrombosis.
Results: THV thrombus formation was detected in 27 (7%) patients. There was no difference in the incidence of THV thrombosis between the Sapien XT and Sapien 3 (8% vs. 6%; p=0.21). THV thrombosis patients had a higher mean gradient at follow-up compared to patients without THV thrombosis (10±4 mmHg versus 8±3 mmHg; p=0.002). Characteristics in patients with vs. without THV thrombosis are shown in the table. 4 of 27 patients developed clinical events attributable to THV thrombosis (stroke, n=1; THV obstruction with heart failure, n=3). Warfarin alone or in combination with antiplatelet therapy caused THV thrombosis regression determined by follow-up MDCT.

	Total study cohort (n=405)	Patients without THV thrombosis (n=378)	Patients with THV thrombosis (n=27)	p value
Age (y), median (IQR)	83 (78–86)	83 (78–86)	83 (79–84)	0.85
Male sex, n (%)	188 (46%)	171 (45%)	17 (63%)	0.06
STS PROM, median (IQR)	5.3 (3.6–7.1)	5.3 (3.7–7.1)	4.6 (3.5–10)	0.75
LVEF ≤35%, n (%)	40 (10%)	35 (9%)	5 (19%)	0.11
Atrial fibrillation, n (%)	188 (46%)	182 (48%)	6 (22%)	0.007
Post-implant warfarin therapy, n (%)	171 (42%)	168 (44%)	3 (11%)	<0.001
THV size				
23 mm, n (%)	88 (22%)	86 (23%)	2 (7%)	0.04
26 mm, n (%)	198 (49%)	186 (49%)	12 (44%)	
29 mm, n (%)	119 (29%)	106 (28%)	13 (48%)	

IQR, interquartile range; LVEF, left ventricular ejection fraction; STS PROM, Society of Thoracic Surgeons predicted risk of mortality; THV, transcatheter heart valve.

Conclusions: In the largest cohort with post-TAVR MDCT follow-up to date, the incidence of THV thrombosis was 7%. Larger THV size and LVEF ≤35% may predispose to THV thrombosis. Warfarin appears to have a protective effect. Although often subclinical, THV thrombosis may have important clinical implications. Future studies are warranted to assess whether tailored post-TAVR antithrombotic therapy can reduce the incidence of THV thrombosis.

1891 | BEDSIDE
Atrial fibrillation is associated with impaired left ventricular energetics that persist despite successful catheter ablation

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Introduction: Atrial fibrillation (AF) is associated with subclinical left ventricular (LV) dysfunction and overt heart failure, but causal relationships are incompletely defined. It is possible that both AF and LV dysfunction are tissue-specific manifestations of an underlying subclinical cardiomyopathy.
Purpose: To investigate the effect of restoring sinus rhythm (SR) and reducing AF burden by catheter ablation on LV energetics, ejection fraction (LVEF) and peak circumferential systolic strain.
Methods: 53 patients referred for AF ablation (63±8y) and 25 age- and gender-matched controls in SR (61±6y) were recruited. Patients had paroxysmal (n=27) or persistent (n=26) AF without coronary artery disease, valvular disease, diabetes, uncontrolled hypertension, inflammatory disease or poor ventricular rate-control.