

ESC 2017 - The corpse of renal denervation starts twitching



[Elizabeth Cairns](#)

Renal denervation, presumed dead in 2014, is starting to show signs of life. Interim results from one of the studies Medtronic began in the wake of its pivotal trial failure three years ago have, for the first time, proven that the technique can lower blood pressure in patients unresponsive to antihypertensive drugs. Medtronic promptly announced plans for another approval trial.

The signs of life are, however, faint. While denervation lowered blood pressure significantly further than a sham procedure, the effect was not huge, at just 5mmHg - too small to be able to say that these patients had their blood pressure controlled. As a result there are questions over whether the benefit is large enough to warrant patients undergoing the procedure.

The Spyral HTN Off-Med trial was started to try to eliminate some of the factors that researchers believe confounded the data in the original pivotal trial, Symplicity HTN-3 ([Decision time for renal denervation firms as Symplicity trial yields little comfort, March 31, 2014](#)). Foremost among these was unrestricted use of antihypertensive drugs: patients in the current study were eliminated if they took medication to lower their blood pressure.

The Spyral HTN Off-Med trial tested an updated version of Medtronic's device, called the Spyral; this has multi-electrodes that deliver more consistent nerve ablation than the earlier model, Medtronic said.

Data from the first 80 patients enrolled in the Spyral HTN Off-Med trial, presented at the annual meeting of the European Society of Cardiology in Barcelona today and [published in The Lancet](#), showed a systolic blood pressure difference of 7.7mmHg between the treatment and sham groups at three months. Medtronic stated that a [recent meta-analysis](#) associated a decrease of that magnitude with a relative risk reduction of approximately 20% for major cardiovascular events, including heart attack and stroke.

All the changes in blood pressure, summarised in the table below, come with p values, but these should be treated with caution at this interim stage.

Interim Spyral HTN Off-Med data				
	Mean decline in BP from baseline (mmHg)			
	Renal denervation (n=38)	Sham control (n=42)	Sham controlled reduction	P value
Office systolic BP	10.0	2.3	7.7	0.016
Office diastolic BP	5.3	0.3	4.9	0.008
24-hour systolic ambulatory BP	5.5	0.5	5.0	0.041
24-hour diasystolic ambulatory BP	4.8	0.4	4.4	0.002

One wholly positive finding was on the safety side: not a single adverse event was seen in either group. Still, this is a small group and an early cut of data.

A difficult case to make

The trial has enrolled 350 patients and will continue until its primary endpoint cut-off of three years. And Medtronic has gone all in already, pushing forward with a larger US approval trial.

Medtronic could not say when this trial might begin, and when it will read out. Its endpoint is unlikely to focus on hard outcomes such as stroke or heart attack rates, however.

“It is likely that our pivotal will target blood pressure reduction as the primary endpoint as this is an accepted surrogate for reduction of adverse cardiovascular events like stroke,” Sean Salmon, president of Medtronic’s coronary and structural heart division, told *EP Vantage*.

The initial promise of denervation was that it could cut blood pressure in drug-resistant patients by something like 30mmHg – this was the kind of figure seen in some early trials with no sham control group.

The drop in the Off-Med study was much lower, and this matters. Discussing the results, Professor Bryan Williams of University College London, put it bluntly: “Renal denervation did not appear to control blood pressure in the patients treated to currently recommended targets.”

As a comparison he summarised data from the Pathway 1 trial of losartan plus hydrochlorothiazide, which enrolled a similar population to the Off-Med trial. This dual drug therapy permitted a blood pressure drop of 19mmHg.

Of the drop in pressure seen with Spyral, Prof Williams said: “I would ask the question, would patients who wish to avoid medication by having an intervention view this outcome as a success?”

He suggested that the technique “could still have a future role in lowering blood pressure in patients with intractable hypertension not responding to medication [but] it’s going to be difficult to present a case that this beats traditional drug treatment.”

Medtronic might have another crack at persuading European cardiologists – Spyral and many other denervation systems are long since CE marked – to pick their catheters back up. Spyral HTN On-Med, in which nerve ablation is used along with drug therapy, is due to report later this year or early in 2018, and a positive result here could add weight to Medtronic’s argument. Interpreting the results may not be straightforward, however.

“Multiple recent renal denervation studies have reported overall adherence to antihypertensive meds of about 50% in similar populations,” Mr Salmon said. “Thus, the added variability in blood pressure outcomes may make it more challenging to demonstrate a statistically significant reduction in 100 patients.”

The US market will have to wait for the pivotal trial, which will doubtless take a few years to yield data. And even if this study is a hit it will have to show a much greater effect size if renal denervation is to make the kind of sales that would move the needle for Medtronic.

This article has been updated with comments from Medtronic.

Trial name	Trial ID
Spyral HTN Off-Med	NCT02439749
Spyral HTN On-Med	NCT02439775

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