The design, development, and testing of an intravascular fluid delivery catheter that can reliably enable three 0.008 in. diameter microneedles to penetrate through the wall of the renal artery without causing bleeding or arterial damage was a major technical challenge. In addition, the needles also needed to have a precise penetration depth of several millimeters outside of the medial layer of the artery in order to ensure that the ethanol penetrates far enough to inactivate the deep-seated sympathetic nerves. The critical components of the design to meet the above criteria are the three guide tubes, which house the needles. These have sufficient structural rigidity to reliably andatraumatically expand outwardly against the intima of the renal artery. Once placed against the wall of the artery, the guide tubes enter the catheter and provide support for the thin microneedles, which can then be advanced through the wall of the artery into the perivascular (adventitial) space.

Figure 1 shows the sequence of use of the Peregrine Catheter with side views on the left and cross sections on the right. Figure 1(a) shows the guide tubes and needles deployed through the wall of the renal artery with the functioning nerves shown. Figure 1(b) indicates the start of infusion of ethanol into the perivascular space. Figure 1(c) indicates the needles and guide tubes retracted back into the Peregrine catheter with the ethanol now forming a doughnut-like spread in the perivascular space surrounding the artery. Finally, Fig. 1(d) indicates the nerves now inactivated by the neurolytic action of ethanol. Note that the alcohol does not penetrate into the (media) wall of the artery itself, enhancing safety.

The microneedles themselves have been constructed to be radio-opaque so they too can be clearly seen here penetrating through the arterial wall into the perivascular space.

3 Results

Upon the completion of extensive preclinical studies [3], a first-human-use evaluation was conducted. The results were very encouraging: Eighteen patients and 37 vessels (one had a accessory renal artery) were treated with 0.3 ml of ethanol in each renal artery using only modest, standard diagnostic cath lab sedation (Versed and Fentanyl at low doses).

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The overall results from the study showed:

- no acute complications: no clots, spasm, perforation, or dissections
- no long term effects on renal function
- arteries appeared unchanged 6 months post-treatment (evaluated by angiography)
- excellent device performance: 100% device success (37/37 vessels)
- brief treatment time: avg. 7 min/artery (range 3–8 min)
- successful navigation to the target site in all renal arteries, including challenging anatomies—short segments and tortuous segments
- a reduction of office-based blood pressure, despite a decrease in antihypertensive medications in the majority of patients
- no/minimal procedural pain, under modest sedation
- when noted, mild, transient discomfort (<1 min)

Baseline and follow-up blood pressures are presented in Fig. 3 for 17 of the 18 patient cohort (one patient passed away from unrelated causes ~2 months after treatment). The results showed a (mean) 23 mm Hg drop in systolic blood pressure in spite of reduction of an average of 1 blood pressure drug.

Furthermore, none of the patients experienced the intensive pain that occurs during RF ablation against the wall of the renal artery. A majority of patients had no pain, those that had pain it was transient (i.e., <1 min).

4 Interpretation

Three factors stand out from the results of the first clinical evaluation of the Peregrine system. First, because there is no capital equipment such as an RF generator and only a single 0.3 ml injection per renal artery, the time and cost for the procedure are projected to be significantly lower than that of RF ablation-based renal denervation procedures.

Second, the pain receptors are located within the inner wall of the artery (the media), and the injected alcohol does not penetrate back, as seen in animal studies, hence resulting in minimal or no pain, and dramatically less than RF procedures.

Finally, because the infusion requires less than 10 mm of vessel length, the Peregrine enables the treatment of shorter length arteries; a critical limitation for RF based devices that require at least a 20–30 mm length renal artery to achieve modest nerve ablation.

In summary, the early results with the Peregrine System are encouraging and now await prospective, sham controlled studies to fully assess the safety and efficacy of the system.

The Peregrine System received a 510(k) clearance by the U.S. FDA for intravascular delivery of diagnostics and therapeutic agents in April 2014. Clinical trials for the European CE Mark have begun, with approval expected in 2015. U.S. clinical studies are slated to begin in 2015.

References