

Clinical Efficacy of Vascular Brachytherapy in the Cath Lab

Greg Braden: We will briefly discuss the clinical efficacy of vascular brachytherapy and review our own local experience, much like what Dean has shown in Christ Hospital. In the case of in-stent restenosis, hyperplasia is really a hyperplastic process. The problem with in-stent restenosis is that predicting target vessel revascularization is very dependent on the length of the restenotic segment. Established biologic and clinical data support radiation use to inhibit uncontrolled cell proliferation predominantly for malignant tumors and for healing scar formation. Scar formation is probably very relevant to the discussions on in-stent restenosis, as it seems to mainly involve scarring within the coronary artery itself. I just received a review from the START trial team, who studied a group of patients randomized to placebo or vascular brachytherapy for in-stent restenosis. An 8-month angiographic clinical evaluation was made. As you are aware, the START trial rather dramatically decreased target vessel failure, target vessel revascularization, and the TVR rates compared to placebo therapy alone. The angiographic restenosis rates were also similarly markedly improved, especially within the area that was treated. Benefits in clinical practice and clinical trials have been shown. Gamma radiation trials and a series of the beta trials which demonstrated improved outcomes with vascular brachytherapy for the treatment of in-stent restenosis. Restenosis rates all decreased on the order of about one-third, or between 31% and 36%. The target vessel revascularization rates versus placebo were reduced again by about one-third; segment reductions were even greater. All of these studies have shown a significant clinical benefit.

At Forsyth Medical Center in Winston-Salem, we started performing vascular brachytherapy with the Beta Cath™ system in December 2000 and through April of this year, we have treated 288 patients, 19% of whom have either multiple lesions or multiple vessels treated at the same time. Although we have not analyzed the data separately, a large number of these patients (79%) actually had debulking therapy as well. Forty-nine of the 288 patients (17%) have undergone repeat cardiac catheterization due to some form of clinical symptoms. And of these, only 10 have had recurrent disease in their treated segments. Some of them have had non-significant diseases elsewhere. Other patients had other diseases not related to in-stent restenosis and underwent subsequent treatment. For a clinical reference, the clinical TVR rates were 3.5% in this initial experience. Two of these patients were actually treated for total occlusion. These are the ten patients who had in-stent restenosis following vascular brachytherapy, two of whom had total occlusions. Two of the patients underwent vein graft treatment. Of these ten patients, nine were treated percutaneous and only one has had a subsequent recurrence, while the other was treated with bypass surgery. Of course many of the 288 patients have not “ripened” yet to demonstrate restenosis. It is important to know that 206 of these 288 are at least six months post-procedure therapy. Again, this represents real world clinical experience with vascular brachytherapy.

Figure 1.

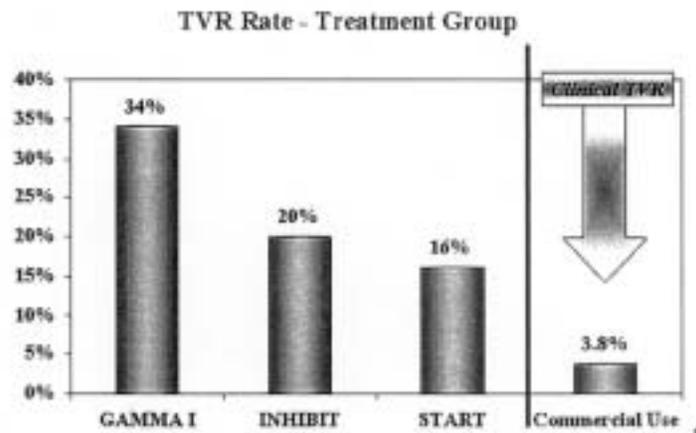
Forsyth Medical Center Experience TVR 3.5%

- 49 of 288 (17%) patients had repeat caths
- 10 of 288 (**3.5%**) had recurrent disease in the treated segment.
- 2 of the 10 pts were treated for total occlusions
- 2 out of 10 pts had SVG treatment
- 9 of the 10 were re treated percutaneously and only one has had a subsequent recurrence, the other was treated with CABG.
- 206 of the 288 are > 6 mo. post VBT

To date, of the nearly 3,700 patients, only 140 have had clinical recurrences for TVR, with an overall TVR rate of 3.8%. Thus we know that vascular brachytherapy works for the treatment of preventative restenosis and for restenosis. It is interesting to note that re-restenosis rates are much higher in clinical trials. Bill O'Neill mentioned earlier that when routine angiographic assessments are conducted, TVR rates similarly increase and when repeat procedures are performed following clinical events, the TVR rates tend to fall, much like in the stent arm of many of the clinical trials. We see this again in commercial use: a 3.8% TVR rate; clinical driven TVR rates with a Beta Cath™ system.

Figure 2.

Let's Talk About The Efficacy of Vascular Brachytherapy



Why these improvements? Part of it has to do with the fact that we now have a better understanding of how to use these vascular brachytherapy devices. We have decreased complications – especially subacute thrombosis – now that we have learned to employ complete regimens to prevent subacute thrombosis. Also, we now have a better understanding of where we need to treat the lesion so we avoid and minimize geographics. The predominant reason for improvements is vascular brachytherapy in clinical and commercial use compared to trials is because we are treating the entire

injured segment of the vessel. Let's talk a little about in-clinic therapy. A number of different studies have demonstrated fairly high subacute thrombosis rates – anywhere from between 4-10%. The duration of in-clinic therapy was generally 30-60 days. The Beta Cath™ trial was the first to extend the length of time of in-clinic therapy for patients undergoing vascular brachytherapy, which resulted in a decrease in subacute thrombosis events. In the stent arm, the rate of subacute thrombosis is much the same between the placebo and treatment arms once therapy was extended to greater than 60 days. Our practice is to treat patients for at least three months with intensive in-clinic therapy. We have experienced no incidences of subacute thrombosis in patients undergoing vascular brachytherapy at our hospital.

In summary, vascular brachytherapy in clinical practice has a very high clinical efficacy rate, partly because we are treating longer segments more completely. An issue could be made regarding better treatment because initially we were not fully expanding the higher pressure balloons. There is clearly a reduction in the occurrence of subacute thrombosis in cases of repeat treatment and over the long-term clinical therapy.

William O'Neill: Thank you very much, Greg. I think you have done a wonderful job of showing how this technique has dramatically advanced from the original trials and become a widely used application. I am very impressed by the consistency of your data. I think Dean showed a TVR rate of approximately 5%, compared to the 3% rate you showed. In our own experience involving 150 patients, the TVR rate was about 2.8%, which is consistent with your data – and I think it is really wonderful news. We do have a very widely applicable, extremely effective treatment for in-stent restenosis. Stephen Ramee will next discuss new approaches and new areas beyond coronary disease.

Figure 3.

William Beaumont Clinical Brachytherapy Experience

- 155 patients treated post-FDA approval with 180-360 day follow-up
- 8 patients with in-stent re-restenosis
- 5 due to geographical miss
- 3 true treatment failures
- TLR 5.2%