Randomized control study of the outback LTD reentry catheter versus manual reentry for the treatment of chronic total occlusions in the superficial femoral artery.

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Authors: R. Gandini¹, D. Morosetti¹, A. Chiaravalloti¹, G. Nano², S. Fabiano¹, G. Simonetti¹, Rome/IT, Rome, IT/IT
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Aims and objectives

The crossing of a chronic total occlusion (CTO) is difficult, often impossible, especially in the case of long lesions. For this reason, after a failed endoluminal attempt, most operators currently use a subintimal approach where the area of the occlusion is crossed within the subintimal space and the true lumen of the vessel is re-entered, distal to the site of occlusion [1].

However, precise re-entry into the true lumen can be challenging for vascular interventionists. Furthermore, this technique presents an increased risk of a distal extension of the dissection to the popliteal artery, of creating an arteriovenous fistula, of compromising collaterals and, in some cases, of excluding the possibility of surgical bypass. For these reasons, a double femoral antegrade and infrapopliteal retrograde approach is sometimes required [2]. This leads to long procedural and fluoroscopy times and raises the risk of complications. To solve this problem, some specific devices have been developed such as IVUS integrated catheters, which consist of a catheter equipped with an intravascular ultrasound transducer, and the fluoroscopy guided Outback Ltd Re-Entry Catheter (Cordis Corporation, Bridgewater, NJ), that consists of a coaxial catheter with a needle that facilitates the process of reentry by introducing a needle across the intima into the true lumen [3,4].

The purpose of this study was to assess the efficacy and safety of the Outback device in patients with a CTO of the superficial femoral artery and evaluate its impact on fluoroscopy and procedural times.
Methods and materials

From October 2006 to March 2007, we performed a single center randomized control study trial on 52 patients affected by TASC II-D superficial femoral artery CTO. Clinical indications for endovascular recanalization were: claudication, tissue loss and at rest leg pain with critical limb ischemia. In the same period, 137 patients with symptomatic femoral artery occlusion were treated and not included in the present study; most of patients were similarly enrolled in different trials conducted in our center, while others declined to participate to this trial.

All eligible patients were invited to participate in the study and informed of their right to withdraw from the study at any time; signed informed consent from each participating patient was obtained before the procedure. The study was conducted in accordance with the current version of the Declaration of Helsinki.

Patients were matched by age, risk factors, and lesions characteristics. Afterwards participants were randomly assigned in pairs using computerized random numbers and were divided in two groups: in group 2, a reentry site proximal to the occlusion was obtained exclusively by the conventional treatment; in group 1, the Outback reentry device was used as unique choice.

The study population was randomly divided into two groups which were statistically homogeneous regarding T1 demographic and clinical features (Table I). In all cases, the length of the obstruction was more than 20 cm and belonged to stage II-D according to TASC Classification [5]; in particular the mean length in the control group was 24.47 cm (SD 2.87) and for the testing group was 25.02 cm (SD 2.30). All patients characterized by lesions classified as TASC A-C, following TASC classification, were excluded from the study. Indications for intervention were: Claudication in 38 cases (18 with outback and 16 without outback), tissue loss in eight cases (four with outback and four without outback), claudication and tissue loss in four cases (three with outback and one without outback), acute limb ischemia in two cases (one with outback and one without outback). Calcifications were observed in all lesions and did not represent a reason for exclusion. Over 52 lesions (26 with the use of the Outback Device and 26 without using the Outback Device), 11 (five with outback and six without outback), presented a severe concentric calcification, 25 (16 with Outback and nine without Outback) presented a moderate calcification, defined as a highly calcified plaque on one side of the vessel, 16 (four with Outback and 12 without Outback) with mild calcifications, defined as focal
sub-centimetric calcifications on one or both sides of the vessel. At the preprocedural diagnostic angiography the below-the-knee lesions were evaluated and afterwards treated; however, the evolution of these lesions has not been considered in the follow-up period. In 19 patients (36.5%), one run-off vessel was diagnosed, in which in seven patients (36.8%) only the anterior tibial artery was present, in six the posterior tibial artery (31.6%), in six the peroneal artery (31.6%). The remained patients presented two or three run-off vessels and a further endovascular treatment was avoided.

In all patients, revascularization was attempted using the subintimal technique but while in group 2, the conventional manual reentry technique was performed to regain access to the true lumen [6,7], in group 1, the OUTBACKVR LTD reentry catheter was used [4,8].

The proximal end of the OUTBACK Re-Entry Catheter consists of a handle with a rotating hemostasis valve (RHV), a flush port for internal device flushing and a proximal braided shaft. The tip consists in a nosecone with two directional radiopaque LT marks allowing correct device orientation. Data about total procedure time, fluoroscopy time and precision in-target re-entry have been collected for all the 52 patients treated.

Technical success was defined as the angiographically demonstrated recanalization with residual restenosis <30%.

Successful in-target re-entry was defined as re-entry into the patent artery within 5 cm from the downstream extremity of the dissected tract. Procedural and fluoroscopy times have been measured starting from the first successful arterial puncture to the moment of removal of the sheath. All Patients completed an up to 36 months followup which included physical examination and Doppler US in order to assess the patency of the treated artery at 3 months interval during the first year and after that every 6 months.

The institutional review board at our institution gave full approval and waiver of informed consent for our study and approved our treatment protocol. All patients gave their written informed consent to both the procedure and the treatment of their personal data.

Procedural time and fluoroscopy time have been compared using Wilcoxon-Mann-Whitney U-test. In-target successful reentry rates have been compared using v2 test with Yates correction.

Statistical analysis was run using R version 2.6.0 open source software publicly available at http://www.r-project.org. All reported P-values were two-tailed and considered significant if less than 0.05.
Technique

All procedures were carried out in an angiographic suite and performed by the same interventional radiologist. In all patients, after an ipsilateral antegrade access with a 6F Glidesheath (Terumo Europe, Leuven, Belgium) sheath was performed, once the proximal end of the occlusion of the SFA was reached, and, we intentionally gained the subintimal space with either a 0.03500 J-Tip Standard or Stiff 180 cm Glidewire (Terumo Europe, Leuven, Belgium) hydrophilic guidewire supported by a 5F KMP Catheter (Cook Europe, Limerick, Ireland). The subintimal position was confirmed by contrast injection and by the loop created by the advancing guidewire.

Once the estimated distal end of the occlusion was reached, in group 2, the re-entry into the true lumen was attempted by directing the guidewire’s tip inward, toward the arterial lumen. However, in those cases in which the characteristics of the vessel did not allow to safely regain the true lumen without extending the subintimal dissection beyond the origin of the popliteal artery, therefore increasing the risk of compromising collaterals and prolonging the procedural time, the interventional radiologist performed a combined antegrade/retrograde approach which consists in puncturing the ipsilateral popliteal artery or an ipsilateral below-the-knee vessel under Doppler guidance and attempting to gain the subintimal dissection created with the antegrade approach or the proximal true lumen. Once this was achieved, the guide wire is then directed into the antegrade catheter which is then advanced into the distal true lumen. Subsequently the retrograde guide was replaced by the antegrade one and antegrade angioplasty was performed. In group 1, once the estimated distal end of the occlusion was reached through the subintimal space, the 0.035 guidewire was replaced with a 0.01400 wire and angioplasty of the subintimal lumen was performed with a 5 mm Admiral (Invatec Medtronic, Roncadelle, Italy) balloon.

The Outback reentry catheter was then advanced over the wire up to the extremity of the occlusion and the LT radiopaque markers of the device were oriented under biplanar fluoroscopy guidance toward the true lumen. The needle was deployed and retracted once the 0.01400 guidewire was confirmed to be inside the true lumen in order to perform balloon angioplasty. Self expanding nitinol stents were deployed in the case of residual stenosis >30%. 2500 UI of heparin were administered during the procedure.
All Patients were administered double antiplatelet therapy consisting in acetylsalicylic acid (100 mg/day) and ticlopidine (500 mg/2/day) starting from 4 days before the procedure to at least 4 weeks.
Results

Technical success was achieved in all cases.

In group 2, the planned in-target re-entry was achieved in 11/26 (42.3%) cases while in the remaining 15/26 (57.7%) patients, the dissection was extended beyond the 5 cm limit but in no case it exceeded the popliteal artery. The technical success rate in group 1 was 100% of cases. In group 1, the in-target re-entry was achieved in 26/26 cases (100%).

In group 2, the mean procedural time was 55.4 ± 14.2 min with a mean fluoroscopy time 39.6 ± 13.9 min compared to 36.0 ± 9.4 min and 29.8 ± 8.9 min, respectively, of group 1. These differences are statistically significant for P <0.0001.

In group 2, the procedure was performed with a traditional antegrade approach in 23/26 (88.4%) cases. In the remaining three cases (11.6%), due to the characteristics of the vessels, a combined antegrade/retrograde approach was necessary and performed by puncturing in two cases the dorsal artery and in one case the posterior tibial artery. In patients in who a double approach was performed, the mean procedural time was 104 ± 14.3 min and the mean fluoroscopy time corresponds to 74.6 ± 10.5 min. In group 2, the mean procedural and fluoroscopy times, calculated in patients treated with the only transfemoral antegrade access, were respectively 49.2 ± 11.3 min and 35.7 ± 10.8 min.

Four (15.4%) stents were deployed in group 2 with respect to 9 (34.6%) in group 1.

No major peri- (within 24 h) or post-procedural complications were recorded in the two groups.

At follow-up one reocclusion was recorded at 6 months, two at 9 months and one at 12 months in group 2. All these patients successfully underwent endovascular reintervention.

In group 1, two reocclusions occurred at follow-up, at 9 and 12 months, respectively, in patients who were subsequently lost to follow up. A further patient was lost to follow up at 18 months with no evidence of occlusion up to that moment.
Fig. 1: Diagnostic angiography documenting an occlusion of the Superficial Femoral Artery with distal rehabilitation at the Hunter's canal through collateral vessels (a-c). Subintimal recanalization of the occluded tract (d). Use of the Outback catheter for the re-entry into the true lumen (e and f). PTA and final angiographic control evidencing the patency of the treated vessel (g and h).

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Fig. 2: Diagnostic angiography documenting an occlusion at the origin of the SFA with distal rehabilitation at the Hunter's canal through collateral vessels (a and b). Subintimal recanalization of the occluded tract (c). Re-entry into the true lumen confirmed by the subsequent angiographic control (d and e). PTA and final angiographic control evidencing the patency of the treated vessel (f-h).

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<thead>
<tr>
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<th>Testing group (n = 26) or group 1</th>
<th>Control group (n = 26) or group 2</th>
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<tbody>
<tr>
<td>Age (years)</td>
<td>65.3 ± 6.2</td>
<td>68.1 ± 5</td>
</tr>
<tr>
<td>Sex</td>
<td>12 male; 14 female</td>
<td>14 male; 12 female</td>
</tr>
<tr>
<td>Mean occlusion extension (cm)</td>
<td>25.02 ± 2.30</td>
<td>24.47 ± 2.87</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>8 (30.8%)</td>
<td>6 (23.1%)</td>
</tr>
<tr>
<td>Smokers</td>
<td>19 (73%)</td>
<td>16 (61.5%)</td>
</tr>
<tr>
<td>TASC Stage IID</td>
<td>26 (100%)</td>
<td>26 (100%)</td>
</tr>
<tr>
<td>Mean Procedure Time (min)</td>
<td>36 ± 9.4</td>
<td>55.4 ± 14.2</td>
</tr>
<tr>
<td>Mean Fluoroscopy Time</td>
<td>29.8 ± 8.9</td>
<td>39.6 ± 13.9</td>
</tr>
<tr>
<td>Success rate (defined as planned in-target re-entry within 5 cm)</td>
<td>26 (100%)</td>
<td>11 (42.3%)</td>
</tr>
<tr>
<td>Success procedure rate</td>
<td>26 (100%)</td>
<td>26 (100%)</td>
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**Table 1**

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Conclusion

CTOs of the SFA have two basic therapeutic options: surgical therapy with bypass tailoring and endovascular therapy.

Traditional surgery is based on bypass tailoring and carries all the risks related to the procedure itself. Traditional open saphenous vein harvest or synthetic bypass graft, which are the commonest surgical procedures to recanalize an occluded superficial femoral artery,

carry higher risk of infectious complications, both along the venous graft origin and to the graft docking site; it involves long skin incisions, and a longer hospital stay. Remote superficial femoral artery endarterectomy, which is a minimal invasive endarterectomy performed through a single femoral arterotomy, the risks remain high, even if still allowing to preserve the saphenous veins for possible future surgery [9]. In terms of endovascular therapy, the optimal treatment would be the intraluminal recanalization of the occluded arterial segment, but, in the case of long occlusions remaining inside the true lumen is extremely difficult. Furthermore the guidewire frequently breaks into the subintimal space, so that for long occlusions intentional subintimal recanalization is considered the first therapeutic option. Many authors reported limb salvage rates to be comparable to those achieved with arterial surgical bypass but with fewer complications. The main difficulty of this technique is regaining access to the true lumen of the patent distal segment of the vessel, beyond the occlusion, due to the often calcified intima. Technical success is limited by the inability to reenter the true lumen in as many as 13-24% of attempted subintimal recanalization procedures [6,7]. In patients in whom the procedure fails, significant medical comorbidity and/or lack of suitable vein conduit may preclude arterial bypass surgery and result in secondary amputation. The 30-day mortality for primary amputation is not negligible.

In those cases in which the re-entry into the true lumen is not achieved close enough to the distal end of the occlusion, extending the dissection too far raises the risk of compromising collaterals, of damaging the popliteal artery precluding the chance of a rescue surgical bypass, or even of perforating the artery and creating an arteriovenous fistula [10]. In some particular cases, re-entry into the true lumen is not possible and a double femoral antegrade/popliteal retrograde approach (SAFARI technique) may be necessary. From this kind of approach, in our facility, we usually use a 21 gauge needle and not a 5F sheath, as reported in many studies, to be less traumatic to the artery.
Furthermore, PTA of the recanalized vessel is performed from an antegrade access limiting eventual small vessels trauma. Even if in our series no complications occurred with this technique, a combined antegrade/retrograde approach increases procedure-related risks such as dissection of the access site, hematoma and arteriovenous fistulas.

Moreover the double approach increases procedural and fluoroscopy times. In a series of 21 limbs, in which the failure to reenter the distal true lumen from an antegrade approach occurred or which presented limited distal target artery available for reentry, Spinosa reported a 100% technical success rate of the SAFARI technique without, however, reporting any data about the procedural time [11]. To gain a precise and swift re-entry to the true lumen two specific devices have been created. One of these is the IVUS integrated catheter which has been reported to be highly effective but involving very high costs.

Saket et al. [12] in their study on 10 patients reported a mean time of 7 min for re-entering the true lumen with this device, without any complication related to the procedure. Kawasaki et al. [13] also reported a high technical success rate of 96% in reentering the true lumen by IVUS guided technique, without complications related to the multiple attempts of re-entering the true lumen with the traditional "hand guided" technique such as perforation of the artery or extension of the dissection far beyond the reentry targeted site. Moreover a significant reduction in use of contrast medium was reported [14,15]. Similar studies reported a high technical success rate, ranging between 64.5 and 96.1%, and failure to achieve the true lumen closely related to the degree of calcification of the reentry site [16-19]. In fact in the study reported by Shin et al. [18], a single observer estimated the degree of calcification, demonstrating a high correlation between the heavily calcified occlusion and technical failure. When there is diffuse calcified disease beyond an occlusion, reentry is usually achieved further beyond, to exclude such pathologic tract of the vessel from the newly recanalised segment. However, this should be done by re-entering as proximally as possible to the site of occlusion, in order to maintain the patency of collateral vessels and target vessels for subsequent by-pass [19]. The re-enter in the true lumen does not represent the only problematic issue, indeed the latter characteristic plays an important role in longterm follow-up because the passage between the subintimal plan and endoluminal space can be characterized
by an increased tendency to elastic recoil and residual stenosis [16]. To avoid complications related to reentry site, using fluoroscopy and road map imaging as guide, in our cases the needle of the Outback was oriented toward the true lumen in the less calcified area. In this setting, the operator experience is fundamental [18]. Some studies reported failure while reaching the true lumen and high complication rates, but suggested that a repeated use is correlated to an increased success rate [17-19]. Moreover, in medical literature, multiple manual attempts to re-entry into the true lumen with a guidewire and a catheter may hinder the true-lumen reentry with the Outback device [17-19], because of a iatrogenic intimal apposition on the opposite vessel side. When using the Outback device after a failed manual true lumen re-entry, in our experience we usually attempt a re-entry in a distal portion of the vessel, where it is reasonable to assume there has been no intimal damage, the vessel is healthier and, thus, more suitable for an outback-assisted true lumen re-entry. Even though several studies reported the use of the Outback re-entry catheter in the treatment of CTOs of the superficial femoral artery, to our knowledge, ours is the first randomized trial to date assessing the efficacy of this device in facilitating true lumen re-entry. In our clinical practice, we prefer the Outback Re-Entry Catheter because of its low profile compatibility sheath (6F), which facilitates the passage in the subintimal space, and its good torque control, which resulted in an excellent effectiveness in the true lumen re-enter and significantly reduced procedural and fluoroscopy times; although the use of the Outback Re-Entry catheter resulted in high procedural costs, these costs are lower when compared to IVUS integrated catheters such as the Pioneer ($1800 vs. $3100) [20]. Moreover, we believe that the low shaft profile allows the placement of arterial access of lower size, thus reducing the risks of retroperitoneal bleedings [17]. Most of the stents were deployed at the passage between the subintimal space and the distal true lumen to grant long term patency. Follow-up data show that there are no considerable differences in the long term patency rates of the treated vessels with both techniques. Regarding the re-occlusions that occurred, we believe they should be evaluated considering both the baseline clinical characteristics of the patients (age, diabetes, and smoke habit) and the length of the occlusions which were among the longest in the study population.
In the case of CTOs of the superficial femoral artery, the OUTBACKVR LTD Re-Entry Catheter in our experience has shown to be a helpful tool granting the accurate re-entry into the true lumen beyond the occluded segment into the patent vessel. Moreover, besides the high reentry success rate, in our series, it allowed a significant reduction of procedural and fluoroscopy times. However, one of the main limits of the Outback LTD is the cost of approximately $1,800 (about € 1400), even if it may vary from institution to institution. Its use is therefore limited [19,21]. The cost increase may be less important in cases in which the antegrade approach fails; in fact in three cases (11.6%) in which a double approach was performed, the endovascular suite was occupied for a mean period of 104 _ 14.3 min associated to an important increase of mean fluoroscopy time and total radiation dose. Besides, the Outback device may help operators with less endovascular expertise in performing a double approach, to obtain technical success with a major reduction of mean fluoroscopy and procedure time. In fact no significant learning curve for the use of Outback device was reported, while a high endovascular experience and skills are required to perform a double approach.

In our experience, the use of this device is very useful for the revascularization of chronic femoral occlusions, even calcific, in which an accurate re-entry cannot be achieved with the conventional subintimal technique. In these cases the Outback device grants high technical success rates and a significant reduction of procedural and fluoroscopy times.


