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Editorial

Unraveling the mystique of CTO Interventions: Tips and techniques of using hardware to achieve success

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ABSTRACT

The scientific discourse of chronic total occlusions interventions is mired in a technical jargon so confusing that it prevents an average interventional cardiologist from pursuing this field so much so that it has become a domain of a few. This review attempts to simplify this vernacular and present it in a manner that this procedure comes within the scope of a mainstream interventionist.

1. Introduction

Interventions in chronic total occlusion (CTO) represent a niche area of percutaneous coronary interventions (PCI). The essential difference lies in the fact that in CTO PCI the disease lumen is occluded (versus patent in a garden variety of PCI). This difference culminates into not only increased complexity and difficulty but also makes it more prone to complications. This situation has led to an evolution of whole new field of interventional cardiology with specialists dedicated to this procedure particularly adept in retrograde techniques. Furthermore, this has led to development of a new jargon of technical words, "reverse CART," "septal surfing," "externalization," etc, a complete new language associated with CTO intervention which has on one hand added to the mystique of the procedure but on the other hand created confusion in the mind of regular interventionists and taken procedure out of their realm. This review is an attempt to clarify and simplify some of the concepts and techniques so that it is easily understandable by regular interventional cardiologists with the overall aim of increasing the popularity and acceptability of these procedures.

2. How is CTO intervention different from a regular PCI?

The essential difference in CTO intervention versus a "regular PCI" is that the lumen is occluded versus open (though stenosed) in a regular PCI. This singularity entails a whole reworking of the entire PCI strategy in CTO interventions. Procedurally, a regular PCI involves the wiring across the lesion supported by a guide-catheter, followed by balloon dilatation (to prepare bed) or sometimes even no pre-dilatation based on severity of disease and type of lesion, followed by stent implantation. However, during the course of procedure several other techniques may also be used like thrombus extraction, distal protection, rota-ablation depending on individual requirements of the case. On the other hand, CTO intervention involves a complex and difficult wiring, followed by a more extensive preparation of bed. Due to this difference the CTO intervention may be associated with slightly lower efficacy and safety but also increased procedure time and use of contrast. Technique wise the PCI in CTO may be different from usual PCI in several aspects:

1. Wiring is usually the key both in terms of technique as well as the characteristic of the wire used, not only to negotiate the

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occluded lumen but also to be able to deliver several types of devices to accomplish a successful PCI.
2. Improved guide support is required to increase the ability to work with a wire.
3. Preparation of vascular bed by pre-dilatation is absolutely mandatory (again because of occluded lumen).
4. There is no classical modus operandi, if one technique is not successful several other variations in technique may be applied: retrograde, parallel wire etc.
5. In a regular PCI, among all the sensory faculties, vision is the most important sensory input with some tactile feedback. However, in CTO PCI this faculty is seriously limited (CTO intervention is essentially a blind procedure – at least in early part), here the tactile sense is the most important. But for human species sight is the most important sense and this being curtailed is the major limitation of CTO PCI. Thus there could be higher value and requirement of alternate imaging like intravascular ultrasound (IVUS).

To summarize, the basic difference between a regular and a CTO PCI is that in a CTO PCI the artery is occluded with no free lumen. But this is not all. This tissue occluding the lumen is of variable consistency, ranging from very soft (micro-channels) to soft (thrombus, proteoglycan, cholesterol clefts) to stiff (collagen or elastin) to very hard (calcium). Table 1 Operationally, to surmount this problem usually more than one wire may be required (chosen according to characteristic of the occlusion) and an individualized strategy has to be worked out. Thus the pre-requisite of a successful CTO PCI involve:

1. Knowing the histology of CTO.
2. Knowing the physical characteristics of the wire and other hardware.
3. Choosing the wire/s or other hardware according to the composition of the occlusion.
4. Knowing how to use the wire/hardware.
5. Choosing the right strategy.

3. Basic histology of coronary artery

3.1. Normal

Coronary artery is composed of three concentric layers: intima, media and adventitia with a central lumen inside. The intima consists of a lining layer of endothelial cells, a sub-endothelial layer containing connective tissue, and smooth muscle cells. Intima is separated from media by a relatively thick but fenestrated layer of internal elastic lamina (IEL) composed of elastin fibers. The media consists of around 40 layers of circumferentially or helically oriented layer of smooth muscle cells and connective tissue (elastic fibers, collagen, proteoglycans). The medial layer is separated from the adventitial layer by the external elastic lamina (EEL) which is composed of interrupted layers of elastin and is considerably thinner than the IEL. The adventitial layer consists of fibrous tissue (collagen, elastic fibers) that is surrounded by vasa vasorum, nerves, and lymphatic vessels. Surrounding bundles of collagen are oriented primarily longitudinally and relatively loosely.

Table 1
Physical characteristic of histological components of occluded segment.

Consistency	Very Soft	Soft	Firm	Hard
Components of Occlusion				
	Re-canalized lumen Micro-channels	Thrombus Proteoglycans Cholesterol clefts Cells	Collagen Elastin	Calcium

3.2. Atherosclerosis

Atherosclerosis is a disease of the intima and is characterized by physiologic disruption of endothelial lining and accumulation of atherosclerotic plaque which may protrude in both lumen and media. Underlying the diseased intima, medial thickness is generally reduced.

3.3. CTO

The characteristic of CTO is an occluded lumen which is initially composed of fresh thrombus but which soon gets organized into loose tissue segments composed of loose fibrous tissue, proteoglycan, haemosidrin/RBC and inflammatory cells intermingled with re-canalized channels. The intimal layer is initially composed of cholesterol clefts, foam cells, giant cell atherophagocyte, RBC, mononuclear cells but gets converted to collagen, elastin and even calcium. In addition there could be neo-vascular channels.[1,2] There are essentially two types of micro-channels:

1. Endothelialised micro-channels (100–500 μ) – They are essentially re-canalized part of occluded artery, and are a CTO operators delight, easily penetrable by a soft, polymer jacketed wire. They are generally present in a recent CTO, in CTOs with a tapered tip; they run parallel to the occluded parent vesseland may span the entire extent of CTO occlusion.
2. Micro-capillaries (<100 μ) – These capillaries are present in adventitia (vasa-vasorum) and may extend into media and intima. They generally occur in older CTOSs, are common with a blunt tip of CTO, run principally in a radial direction, do not connect proximal and distal caps, and are predisposed to subintimal passage Fig. 1.

In addition at both ends of CTO there is accumulation of dense collagen rich fibrous tissue known as fibrous cap. The cap is likely to be stiffer, more extensive proximally as compared to distally because of flow characteristics of an occluded artery.

4. Properties of guidewire in context of CTO PCI

Depending on its construction guidewires have different properties which can be used to an advantage in different situations.[3,4]

4.1. Penetrability

Penetrability is the ability to puncture a lesion, the stiffer the lesion the more penetrability is required; wire in the lumen < micro-channel < lipid plaque < proteoglycan < collagen/elastin < calcium. The penetrability of a wire depends on its:

1. Tip load
2. Tapered tip
3. Wire support (micro-catheter/OTW Balloon, anchoring techniques, child-in-mother catheter)
4. Lateral support of the wire

4.2. Pushability

Pushability is the amount of force needed to advance the wire or the ease of advancing the wire once it has penetrated a lesion. Pushability depends on a) the characteristic of the tissue a wire has

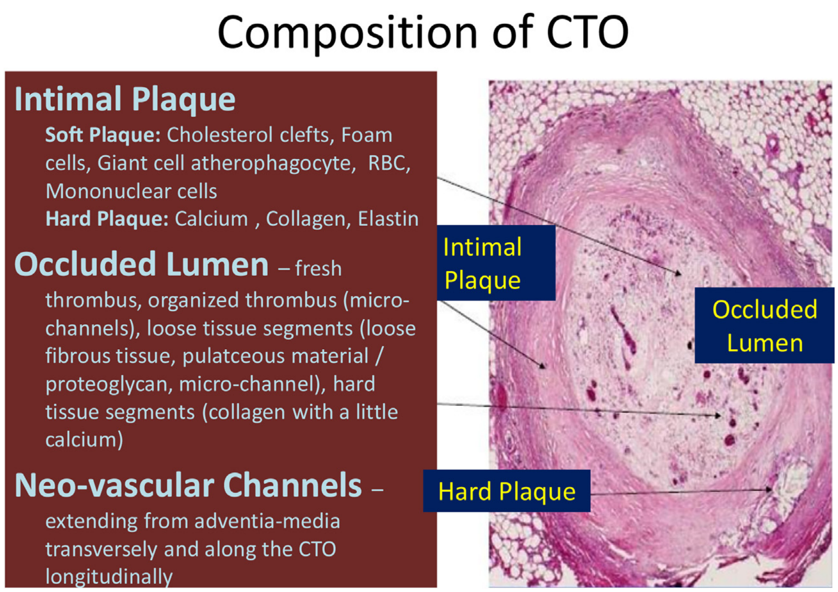

Fig. 1. Histology of occluded lumen in CTO.

to traverse as well as the b) length of the tissue to be traversed along the CTO. This feature is determined by the lateral support provided by the wire.

4.3. Trackability

Trackability is the ability of the device to track over a guidewire during insertion especially around bends. This feature is determined by the lateral support provided by the wire.

Torquability (1:1 transmission of bend)

Steerability is the ability and responsiveness of the wire tip to navigate vessels and torquability is the response of the wire to turning by the operator when navigating vessels (the ability to transmit torque from the proximal end to the distal end of the wire). This property is important in drilling strategy where wire is rotated in a controlled manner to search for path of least resistance. It is improved by:

1. Single core wire – force transmission is not dampened by the terminal coil.
2. Higher lateral support provided by the wire.
3. Specially designed wires capable of torque transmission (wires with dual or composite core).

4.4. Bending

Ability to bend is required to circumvent a very stiff tissue e.g. calcium. Coil structure at the end of the wire allows for this property (while single core wire resists it).

4.5. Lubricity

Resistance is encountered while moving the wire in a vessel or through any lesion. Lubricity is the ease of this passage. The resistance encountered depends on

1. The tissue encountered: vessel lumen << micro-channel < lipid plaque < proteoglycan < collagen/elastin.
2. Bends (tortuous lesions)
3. Length of the lesion

In general resistance offered is as follows: polymer coat < hydrophilic < hydrophobic < non coated.

5. Elements of a successful PCI

The success of PCI in CTO lesion depends on careful analysis of the case and the strategies to be applied even before starting the case. Careful assessment of anatomy using orthogonal views of cine angiography, utilizing contralateral injections (if filling the distal stump), even multi-slice CT or IVUS may be extremely helpful. Likewise calculating the maximum contrast and fluoroscopy time permitted is essential. Finally, the knowledge and experience in using specialty hardware: guide-wires, micro-catheters and IVUS is critical. Tips and Techniques 1& 2 Employing strategies to limit the use of contrast may be especially useful when planning complex procedures and in patients with renal dysfunction. Tips and Techniques 3 However one of the key factors in any successful CTO PCI is to know when to stop and bring again the patient later. Tips and Techniques 4.

6. Strategy for CTO PCI

6.1. Identifying course of the occluded artery

The first step in undertaking PCI of CTO is to understand the course of the occluded artery. The aspects of the occluded segment will have a bearing on strategy to be employed, hardware to be chosen and ultimately success. Thus the course of occluded artery needs to be accurately clarified using various imaging techniques. Tips and Techniques 5.

6.2. Access route

One can access CTO via either femoral or radial route but femoral route may be preferable because for employing some set-up:

1. 8F access may be optimal when
   - Double micro-catheter technique (See-saw) is employed during antegrade approach
   - IVUS catheter is used during the procedure (IVUS + CTO hardware)

– Venture catheter is used
2. 7F access may be useful for
– Use of CrossBoss™ device and some other bulky hardware – Anchor balloon technique – stent graft is required
3. 6F access may be chosen by experienced operators when use of bulky hardware is not anticipated

6.3. Use of anti-thrombotic anti-platelets

Potent anti-platelet agents like direct thrombin inhibitors (bivalirudin) or GpIIb/IIIa antagonists are generally avoided. Anti-coagulation with un-fractionated heparin (UFH) is preferred because of its easy reversibility in case of perforation. For antegrade technique an initial activated clotting time (ACT) of <200 s (sec) is optimal until the wire crosses the CTO lesion. After crossing an ACT of 250–300 s should be maintained. However, for retrograde technique an adequate heparinization (>300 IU) is a must in view of risk of donor artery thrombosis with inadequate anticoagulation.

6.4. Guide support

Guide-catheters with side-hole may be preferred especially in RCA CTOs. Choice of guide with higher support is essential because guidewire is required to be pushed across a completely occluded lesion. Better guide support can be achieved by a variety of techniques: larger guides, more co-axial placement, better supporting guides (EBU, XB, Amplatz etc), deep-seating of guide, using stiffer buddy wire, balloon anchoring, using smaller guide inside main guide, child in mother guide catheter or encasing the guide with a long sheath (≥30 cm).[5]

For retrograde approach a short guide (80–85 cm) and 7F size may be ideal.

6.5. Guide wire

The next step is choosing the right guidewire. Guidewire choice and handling may be the most important step in CTO PCI because most failures are associated with failure of guidewire crossing. How the wire is chosen and subsequently handled depends on what wire strategy is planned. In general a wire can be advanced in the occlusion in any one of the three ways: [1,3,4,6,7]

1. **Sliding technique:** This technique is utilized in younger, relatively softer tissue composed of loose fibrous tissue, proteoglycan, haemosidrin/RBC and inflammatory cells inter-mingled with re-canalized channels. Generally all it requires is a wire with slightly higher tip load (tip load 1–2 gm) – “soft” unlike a “floppy” wire (tip load ~0.7) used for regular PCI with a flowing lumen. Another requirement is a wire which has a relatively high lubricity or lower friction (hydrophilic or polymer coated) because the wire has to traverse through an occluded segment with relatively high resistance to wire passage. Slightly higher lateral support (~10) is also desirable to enable smooth device delivery unless the lesion is extremely well prepared. Example of such a wire is Fielder XT-A/FC, Pilot 50 which can seek out micro-channels spanning the entire extent of CTO. Wire escalation to a higher tip load wire (safest to less safe) and higher penetration power can be used as required till the CTO crossing is achieved. This technique may not require increased guide support, intravascular imaging or any other special technique or hardware, the only special step required is the vessel preparation prior to stent placement. This kind of wire handling has also the lowest risk of getting sub-intimal and perforating.
2. **Drilling Technique:** This technique is utilized when CTO segment is composed of a stiffer tissue; collagen, elastin or even calcium with a variable amount of softer components. The technique is a fast but controlled rotation of wire through 360° but only a gentle advancement, somewhat akin to a drilling of a bore-well. The hardware for performing this technique involves a wire with a higher tip load (3–12 gm) with/without taper, higher lubricity and higher lateral support. Miracle or Conquest series of wires are the ideal choices. This technique may also require a higher guide-catheter support; larger bore guide catheter, buddy wire, buddy balloon, use of OTW balloon catheter/micro-catheter, or even child-in-mother catheter. Preparation of the lesion is absolutely mandatory. Use of additional imaging modality like IVUS may also be useful.
3. **Penetrating Technique:** This concept involves forcing the wire through the obstruction like a screw. The rotation movements are smaller (45° – 90°), the forward penetration force is higher and the wire is stiffer with / without a tapered tip (Miracle 12, Conquest Pro 9, 12 or 20).
4. **Push and Torque Technique:** This is the most modern technique. The wire used is intermediate but highly torqueable like Gaia 1, 2 3, or Next. In contrast to drilling this technique involves pushing the wire with force but only gentle rotation and waiting for the wire to acquire requisite position. The concept involves negotiating the wire through a tissue till it encounters a tough histological structure like a bundle of collagen, or elastin or even calcium; then redirecting the wire around the tough obstruction into another plane of softer tissue and so on and on forwards longitudinally. If it is not possible to maneuver around the tough tissue the wire is slightly withdrawn and maneuvered into a different plane. If however, it is still not possible to circumvent around the tough tissue, the wire is left in place and a new wire is taken, taking a different route and same technique employed with the new wire (Two wire techniques). The essential requirement here is a wire of moderate tip load (1.5–4.5) but more importantly 1:1 torqu-ability, to be able to redirect wire at will (if torque is not transmitted, the wire may form a clump at the tip and loose its penetration). Other requirements are a higher lateral support. In this context wires with consistent torquability may be more useful like Gaia™ wires. They utilize a composite core technology which allows a greater directional control without compromising on penetrating power. This tactic also requires a higher guide support and careful lesion preparation after crossing with wire. However, despite all this it may be difficult to penetrate the tissue especially if there is a lot of calcium. Therefore in some cases an alternate technique; sub-intimal tracking, retrograde etc may be required. Further, there is a risk of penetrating through the elastic lamina (elastin) to reach sub-intimal space or even perforate out of the vessel. Thus not only tactile feel but an exact knowledge of anatomy is critical to it; prior CT image and use of intra-procedure IVUS may be very helpful.

All the four methods work on the broad principle of wire escalation which involves the exchange of a wire with lower tip load with a one with higher tip load and penetrability if resistance is encountered. This strategy may be aided by use of either over-the-wire (OTW) balloon or a micro-catheter. Here micro-catheter is preferred over OTW balloon because not only it provides more support to wire but also allows wire to be delivered to exactly same point.

7. CTO approaches

There are two basic approaches to a CTO PCI: Antegrade or Retrograde.[1,7] In majority of cases an antegrade approach is the first choice unless certain anatomical features are present which may favor an initial use of retrograde technique. Tips and Techniques 6 The steps involved in antegrade PCI include; negotiating the fibrous cap, advancing the length of occluded segment, penetrating the distal cap, re-entering the distal true lumen, preparation of occluded segment and finally stent implantation. While undertaking the penetration of fibrous cap and negotiating the occluded segment 3 basic approaches; antegrade loose tissue tracking, antegrade intimal plaque tracking and antegrade sub-intimal tracking are employed. The steps in retrograde PCI include: traversing the donor segment, traversing the collateral, crossing the occluded segment, externalization (if retrograde wire is used for crossing), occluded segment preparation and finally stenting. While crossing the occluded segment 5 main approaches are utilized: kissing antegrade wire cross, retrograde wire cross, controlled antegrade-retrograde sub-intimal tracking but crossing with antegrade wire (CART), reverse CART (controlled antegrade-retrograde sub-intimal tracking but crossing with retrograde wire) and knuckle wire technique (KWT).

7.1. Antegrade

Knowing the characteristics of guide-wire and their appropriate use is crucial in performance of antegrade technique. The technique of using guidewire involves; shaping of guidewire (Tips and Techniques 7), appropriate choice of guidewire strategy (sliding, drilling, penetration or push and torque), handling of guidewire (Tips and Techniques 8) and finally tactile appreciation i.e. whether the guidewire is in true lumen, or in sub-intimal space or extravascular space. When wire is in sub-intimal space there is resistance in advancement, relative resistance during withdrawal but free tip rotation. Wire shaping is another specialized skill in CTO intervention. The tip curve depends on the field the wire is employed; in regular PCI, for ideal performance, the tip bend should be equal to the diameter of the vessel. However, in CTO PCI during fibrous cap penetration since the vessel is completely occluded with only a very small tip or dimple, the bend should be minimal (≤1 mm). Once the wire perforates the cap and enters the occluded lumen the playing field increases somewhat and so a broader bend is employed (2–5 mm from the tip).

7.1.1. Perforation of fibrous cap

The first step in perforating the fibrous cap is the identification of the tip. For this the stump should be evaluated in orthogonal views on cine angiography. If the stump is flat then a seasoned operator "looks for a dimple" or even may even utilize IVUS (Tips and Techniques 9). Once dimple is located, the wire forward push is maintained and the wire tip is rotated 180° to penetrate the cap. For achieving all this a wire with a higher tip load (Gaia or tapered tip) is required, which is always maintained co-axially (center of the lumen). One of the techniques outlined below should be utilized to achieve success:

1. **Antegrade loose tissue tracking:** Technically this is the simplest of all CTO techniques and it is generally utilized when the occlusion is relatively younger and the lumen segment is composed of loose fibrous tissue. All this method requires is a soft wire (tip load ~1) with a hydrophilic or a polymer coat like Fielder FC™ wire, which slides through this tissue picking up re-canalized channels whenever it encounters them. However, if the first wire fails, wire escalation may be required.
2. **Antegrade intimal plaque tracking:** This technique relies on the fact that intimal plaque (in contrast to lumen) may be composed of cholesterol clefts, foam cells, giant cell athero-phagocyte, RBC, mononuclear cells admixed with some amount of collagen, elastin (rarely calcium). Some neo-vascular channels may also be present traversing variable length of occlusion. Here again initially a soft wire with hydrophilic/polymer coating may be useful to steer/slide through the intimal soft tissue and traversing neovascular channels when they are encountered. The elastic layer of IEL prevents the soft wire from crossing into sub-intimal space of media and thus this technique has minimal chance of perforation. Over a period of time when this loose tissue gets organized into fibrous tissue interspersed with calcium, a soft wire may not be enough. Again a wire escalation technique utilizing a wire with a higher tip load (1–4), higher lubricity and higher lateral support may be necessary to follow-through slightly stiffer lesion employing a drilling strategy. Further, since it has to penetrate the tough tissue, a wire wherein the distal tip tapers to a narrower profile; 014 wire tapering to 010 (Cross IT™) or 009 (Fielder XT™) may be a good choice. However, since this wire can penetrate through rather tough tissues this wire has some probability for penetrating both elastic lamina and reach extra-vascular space or in other words perforate. Thus when the wire hits a relatively tough tissue; bundle of collagen, elastin or even calcium, the best scenario is not to try force it but rather change course and move in a new direction, using torquable wires (Push and Torque strategy) such as Gaia wire. However, in long-standing CTOs the intimal tissue may get completely converted predominantly into bundles of tough fibrous tissue. Here, further escalation of wire with higher tip loads (6–12) will be required to penetrate through the lesion. Typically, Miracle™ or Conquest™ wires are the only wires that will work in this situation. However, these wires lack in torquability and carry the highest risk of perforation. The risk increases more so if tactile feel is lost as a result of hydrophilic coating or even further lost with polymer coating, Thus, to decrease this risk of perforation somewhat Conquest Pro 12™ (a wire with a very high tip load 12) has the distal most tip uncoated to provide for tactile feel. Further, in tortuous lesions it is difficult to visually make out when the wire crosses into extra-vascular space. In this situation wires with above characteristics (hard, high lateral support) minus the penetrating tip i.e. with a non-penetrating tip are more useful; Miracle Bros™ 3–12. Entering into sub-intimal space remains a distinct possibility and factors predisposing to this eventuality should always be kept in mind. Tips and Techniques 10
3. **Antegrade sub-intimal tracking:** This technique may be sometimes employed in longer standing CTOs where the occluded lumen as well as intimal tissue gets converted into tough fibrous tissue. One approach is to use a drilling strategy using a penetrating wire with a higher tip load. However, this is fraught with risk of perforation. An alternate strategy is to use a medium wire and cross the IEL into the sub-intimal space, carefully slide through the soft sub-intimal space throughout the entire extent of CTO and cross back into true lumen once the entire blocked space traversed. The success of this approach depends on 2 essentials; first the ability to cross back into true lumen when desired and second the ability to prevent crossing the EEL into extra-vascular space. Thus the crux of this technique is the ability to cross into and out of any space at will, a feat difficult to achieve in view of limited visual and tactile guidance. A very important precaution with this technique is to avoid vigorous antegrade contrast injections as much as possible because they can lead to enlarging of the sub-intimal space and obscure visualization of distal true lumen. It is better to use retrograde contra-lateral injections

instead. The classical technique was the sub-intimal tracking antegrade re-entry (STAR) technique which used the bended (knuckle) antegrade wire to achieve safe and predictable opening of sub-intimal space but now several modifications of STAR technique are available.[7] Table 3 Recently Cross Boss™, Sting Ray™ device has been used for controlled sub-intimal tracking and re-entry. The aim is to traverse the enter body of CTO in the sub-intimal space in the safest possible way and then re-enter into distal true lumen by use of dedicated re-entry device. Currently, there are 2 specialized hardware to achieve this goal: The CrossBoss™ is actually a metal OTW micro-catheter with a very soft, non-penetrating round tip, used to safely traverse the sub-intimal expanse over occluded CTO. The device can be rotated in either direction and is advanced without a wire sitting in it. CrossBoss™ manipulation is very important; there should be an adequate guide support, gentle forward traction is applied, focused in one direction, the device moving forward by rapid spinning motion of the fingers, keeping as close to true lumen as possible. Once the entire length of occlusion is traversed, it is exchanged over a wire with Sting Ray™ balloon. When inflated this balloon assumes a flat shape (which is non-damaging) and allows orientation of the penetrating wire (Sting Ray™ wire) towards the true lumen. It does so by virtue of having 2 exist ports opposite to each other with a radio-opaque marker just distal to the port to mark its orientation towards the true lumen. The port which is oriented towards the true lumen is chosen to pass the Sting Ray™ wire which is a tapered wire with a high penetrating force. Once it enters into true lumen the whole apparatus is removed and the channel created used to pass a regular penetrating CTO wire and cross into the true lumen. Finally, this wire is exchanged for a regular work-horse wire and the procedure is completed over it.

7.1.2. Traversing the length of CTO

After penetrating the proximal fibrous cap, the wire (over a micro-catheter) can be exchanged for a wire with lower tip load (Gaia™) and a push and torque strategy employed, utilizing micro-catheter support. Contrast injection immediately distal to proximal cap of CTO may identify and enlarge micro-channels creating a passage-way between proximal and distal true lumen.[7] On the other hand, entering sub-intimal space remains a distinct possibility and therefore all possible strategies must be undertaken to avoid this outcome. Tips and Techniques 11.

7.1.3. Piercing the distal cap

Once the lesion length is traversed, distal cap is to be pierced. At this point guidewire is exchanged for a stiffer, penetrating wire (Conquest Pro™) with lesser bend and angle. It is important to keep the wire in the center of the lumen on the mural side and obtain orthogonal views on phase-adjusted antegrade and contra-lateral injections to clarify the distal fibrous cap and distal true lumen. Micro-catheters provide good support for penetration but in case of difficulty of passing a regular micro-catheter near the distal cap, a Tornus catheter may be used. Sometimes parallel wire strategy or even IVUS guidance may be required to pierce the cap. This part also carries an additional risk of sub-intimal entry.

7.1.4. True lumen entry

As soon as the wire enters the lumen there is a distinct tactile feel. Tips and Techniques12 Once stiff guidewire crosses the fibrous cap and re-enters the distal true lumen, it should be immediately exchanged with a floppy wire and the rest of the procedure carried out over it.

Wire crossing but balloon not crossing

In majority of cases the success in a CTO PCI depends on crossing with the guide-wire but in minority the wire crosses but the balloon is unable to cross. Here several options are available from increasing the guide catheter support, to using a heavier duty wire, to use of rota-ablation or laser but some simple techniques such as wire cutting technique, seesaw balloon wire cutting technique or sub-intimal distal anchor techniques can also be employed.[7]

8. Retrograde

Philosophically, the technique is based on the premise that it is easier and safer to cross fibrous cap retrogradely than antegradely. The reason why it is easier to cross retrogradely is because proximal cap is more likely to be fibro-calcific than the distal cap as also having a blunt stump with side-branch (SB). On the other hand with retrograde approach. SB is not encountered during beginning of fibrous cap penetration (as one classically does with antegrade technique). Further, it is safer during retrograde approach because even if there is sub-intimal penetration the space is not enlarged by a forward flowing blood (as it would be with antegrade technique). Procedure wise, the overall aim of this technique is, first to connect antegrade and retrograde channels and second to keep the connection as close as possible to proximal or distal fibrous cap. The basic technique is that first a soft wire is inserted into the donor artery (not CTO containing artery), negotiated through an appropriate collateral into the target artery retrogradely. Once the wire reaches the site of obstruction (distally - the distal cap), the soft wire is exchanged over a micro-catheter for a stiffer wire. The CTO is then crossed with one of the strategies described below. The underlying principle of the whole technique is to switch over to antegrade procedure as soon as possible. Technique-wise, one essential difference (vs. antegrade technique) with retrograde method is that a huge distance of relatively normal segment is encountered before the penetrating hardware can reach the site of obstruction (distal fibrous cap). This can be achieved by a couple of modifications in the hardware: One, the donor guide can be of shorter length (80–85 cm) and higher profile (7F) whereas other hardwares like sheath, guide-wire, balloon catheters, micro-catheters be of longer length. Typically, retrograde guidewire is of a longer length (300 cm). Second, the hardware should be safer because it has to confront huge distance before it can even reach the site of interest i.e. the obstruction. Finally, the material should have less friction and lower profile (010 guidewires).

8.1. Traversing the donor artery

In context of guidewires it translates into longer wires (300 cm), with lower tip load with hydrophilic/polymer jacket coating. Thus first wire chosen is one with either very low tip load (but sufficient length) such as Sion Blue™ (a tip load of 0.5) or better still polymer jacket coated (but still having a low tip load) such as Fielder XT-R™ (tip load 0.6) or Sion Black (tip load 0.8). Other wires of Fielder series like Fielder FC™, Pilot™/Whisper™, Runthrough™ or Choice PT™ can also be used but have a somewhat higher tip load. Regarding the micro-catheters the essential requirement is again a low profile but other requirements such as pushability, support and channel dilation are also important. Finecross has the lowest profile but poor pushability support. Corsair™ has better pushability and support and can act as channel dilator as well but at a cost of slightly higher profile. Tornus™ on the other hand has maximum pushability and may provide anchor to both guide catheter and wire once it enters the lesion. It however, is prone to cause more damage.

8.2. Negotiating the collateral channels

The second step in Retrograde CTO intervention is negotiating the collateral channel. Since this step involves crossing a channel which although non-diseased is of a narrow caliber and thus likely to be injured (perforated/dissected) during the process of hardware passage, every care should be taken to prevent its injury:

1. Using low profile hardware
2. Choosing a safer collateral: In descending order of safety – SVG graft > septal collateral > epicardial collateral > internal mammary graft. Compared to epicardial channels, septal channels are straighter, with multiple branches, less prone to rupture and even if they rupture the rupture is generally self limited without a catastrophic outcome. On the other hand epicardial collaterals are more tortuous, and more prone to rupture and procedural ischemia.
3. Straight collateral is safer than tortuous

8.2.1. How to cross a collateral channel

While choosing a septal channel connectivity and course (straight or otherwise) are important considerations. Wire and other hardware should be advanced in diastole (collateral size is larger in diastole). There are two techniques of crossing a septal channel: "Septal Surfing," a blind technique, without contrast guidance and another one with contrast guidance. The method involves removal of guidewire from micro-catheter while dripping saline over the hub followed by aspiration of any air from micro-catheter and subsequent direct injection of contrast being delivered through the micro-catheter. The wire should freely advance in the collateral; difficulty in advancing the wire may be indicative of perforation and whipping motion of wire tip may suggest an LV or RV entry or even migration to pericardium. Besides wire crossing another requirement is septal channel dilatation. For performance of PCI via retrograde route, the collateral size should be large enough to pass balloon catheter (so that the occluded segment can be dilated retrogradely). This may require channel dilation using a small balloon (<1.5 mm) dilated at 1–2 atm. However, some micro-catheters can act as channel dilators; If Corsair^{TM} or Tornus^{TM} is used to negotiate the channel, by virtue of their structure (tapered tip to larger shaft) and use (screw like advancement) they can automatically cause channel dilation. On the other hand, if epicardial vessel is the chosen, collateral channel size is the most important criteria. Further, with epicardial vessel, dilation should not be performed (because it is generally already large and is prone to damage and perforation).

8.3. Penetrating the occluded segment

The third step in retrograde CTO is crossing the occluded segment. The retrograde technique is named after the technique used for this step.[1,8–10] The aim of this step is to cross the body of CTO in the safest possible way. Generally, retrograde wire escalation strategy with use of micro-catheter is safest (retrograde

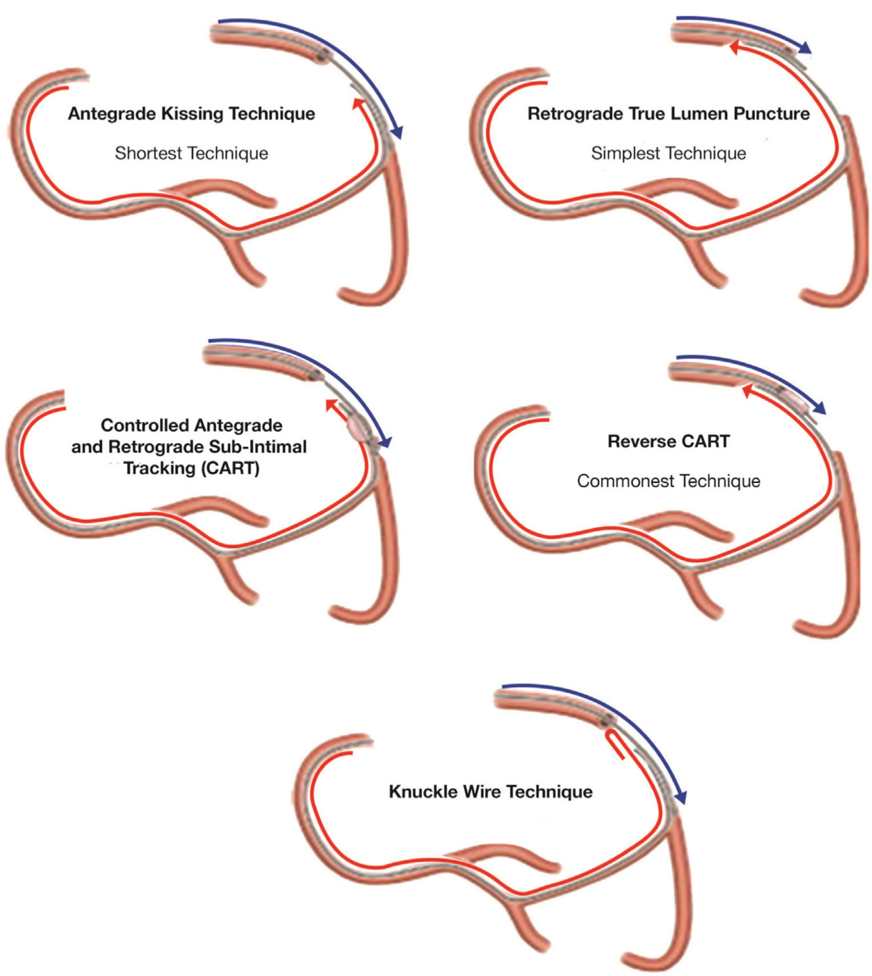

Fig. 2. Retrograde CTO approach.

true lumen puncture). Here again Gaia^{TM} wire may be very useful. If this technique is not possible then antegrade wire is passed into proximal lumen (antegrade kissing technique) Fig. 2.

1. **Antegrade Kissing Technique** – This is the shortest possible technique. Here both the antegrade and retrograde wire are in true lumen and the CTO segment is crossed antegradely using the tip of retrograde wire as a marker. This technique is generally more difficult than the second technique (because proximal fibrous cap is more difficult to penetrate).
2. **Retrograde True Lumen Puncture** – This is the simplest of all techniques. Here again both the antegrade and retrograde wire are in true lumen. First, the anterior stump is balloon dilated, which expands the antegrade channels and increases the chance of retrograde wire finding antegrade lumen. Then retrograde wire is advanced into the true lumen with antegrade wire acting as the marker(for true lumen). The retrograde wire is then advanced into antegrade guiding catheter.
3. **Controlled Antegrade and Retrograde Sub-Intimal Tracking (CART)** – Here to begin with antegrade wire is intimal but retrograde wire is sub-intimal. This is the least favorable of all techniques because if pursued to its logical conclusion, it will involve dilatation of retrograde sub-intimal space with a balloon catheter which essentially would entail passage of bulky balloon catheter (1.5–2 mm) via retrograde route through the septal/epicardial channels with some likelihood of their damage. Antegrade wire is then used to pierce this retrograde sub-intimal space and then guided by inflated retrograde balloon to enter into true distal lumen.
4. **Reverse CART** – This is the most utilized technique in the modern era. Here antegrade wire is sub-intimal and retrograde wire is intimal. This may happen by chance or deliberately when antegrade wire is entered into sub-intimal space with limited extension to span the entire expanse of obstruction. Subsequently there is intentional aggressive antegrade balloon dilatation to attempt to disrupt the body of CTO and open up a passage for retrograde wire entry into true lumen. The retrograde wire is directed to enter this space and then into distal true lumen beyond the obstructed segment.
5. **Knuckle wire technique (KWT)** – This is similar to CART technique but instead of dilatation of retrograde sub-intimal space with bulky balloon, a knuckle is formed by buckling of retrograde wire (a polymer coated wire) and this buckled wire enlarges the retrograde space. Subsequently antegrade wire can cross into retrograde sub-intimal space and then guided into true distal lumen. A modification of this technique is double knuckle wire technique.

Each of these techniques has its own advantages and disadvantages. Table 2 Chance of success is highest with reverse CART but the procedure is technically most challenging as well. There have been several innovations in trying to make this technique simpler; balloon inflations in sub-intimal space (Tips and Techniques 13) and wire trapping techniques (Tips and Techniques 14). Another technique greatly simplifying reverse CART procedure is the “Rendezvous Technique.”The technique involves end-to-end alignment of retrograde and antegrade micro-catheter within the smaller curvature (primary bend) of antegrade guide. The antegrade wire is used to secure the connection between two abridged micro-catheters and is then advanced beyond the occluded segment (in the retrograde micro-catheter) into the distal true lumen, right into the collateral channel. Once the antegrade wire is in collateral channel, retrograde hardware may be carefully removed but it may be better to leave micro-catheter in the collateral. Premature removal of retrograde hardware before completion of antegrade procedure may lead to collateral transaction with possible rupture in middle of the procedure. The antegrade wire is then withdrawn from the collateral channel and appropriately positioned in the true lumen distally (beyond the occluded segment). Finally, PCI via antegrade route carried out in a regular manner. It is important to re-emphasize that with any of the technique, if antegrade wire crosses into true lumen, the retrograde micro-catheter should still be kept in place till the whole PCI procedure is carried out antegradely.

8.4. Externalization of retrograde wire

This is generally the fourth step, if it is the retrograde wire that has crossed into true lumen. The concept is that if stent implantation is attempted via retrograde route it is very difficult, virtually impossible because the stent must be delivered through the tortuous tiny channel in retrograde fashion, even dangerous. The basic technique is that the retrograde wire is used to wire the antegrade guiding catheter and brought out of antegrade sheath. Then PCI hardware is loaded over it antegradely to complete the procedure. The crux of the matter is that a special type of wire is required for this

Table 2
Advantages and dis-advantages of various retrograde techniques.

Technique	Advantage	Disadvantage
Antegrade Kiss	Simplest	Very low success rate (difficult to penetrate proximal cap)
Retrograde Kiss	Simpler than CART techniques	Low success ~20% (it is difficult to get 2 wires in the same plane)
CART	Successful in some cases	Risk of injury to collateral channel by retrograde balloon); sub-intimal space can extend proximally (risky with ostial LAD because then it can cause left main dissection
Reverse CART	Success rate highest Possible to use IVUS Larger balloon can be inflated in antegrade space Retrograde wire easily trapped in antegrade lumen	Technically most complex; Long antegrade sub-intimal dissection along course of occluded artery; collapse of connecting channels can happen intra-procedure antegrade intima-medial disruption may be difficult; two sub-intimal spaces may be mal-aligned externalization of wire has to be performed
Knuckle Wire	Fair success rate; Unlike CART no need for retrograde balloon dilatation	Retrograde dissected space may not be controlled; cross-sectional dissected area (by knuckle) may not be adequate to allow antegrade wire to penetrate it

Table 3
Techniques of antegrade sub-intimal tracking.

1. STAR Technique – it requires the hydrophilic wire to form a tight loop at the tip of the wire (knuckle) and this knuckle is advanced in the sub-intimal space from the proximal true lumen to cover the entire span of occluded section to reach distal true lumen, where it is straightened to re-enter in the true lumen.
2. Contrast guided STAR – in this technique pure contrast is injected via the micro-catheter/OTW balloon. The contrast extends the sub-intimal space to reach near the true distal lumen.
3. Mini STAR – here-in two curves are fashioned on the antegrade wire; first curve 1–2 mm from the tip at an angle of 40–50° and the second curve 3–5 mm proximal to tip at 15–20°, this curve used to cross the occluded segment and then re-enter in the true lumen.
4. LAST Technique – this technique is like a mini-STAR but instead of hydrophilic (like Fielder ™ wire), a Conquest Pro™ or Pilot 200™ wire with an acute bend is used.

retrograde cross-over to the opposite sheath (externalization) since the original wire used to penetrate the distal fibrous cap is too short for externalization and has to be replaced with a wire 300–330 cm long. Thus exchange has to be performed over the retrograde micro-catheter which has crossed the extent of CTO body and is now positioned into antegrade true lumen. RG3 is one such wire which is not only 330 cm long but also a thinner (010) and safer but with good lateral support to deliver PCI devices.

8.4.1. How to do externalization

1. Introduction of retrograde wire into the antegrade guide catheter.
2. Retrograde micro-catheter is then advanced into the antegrade guide catheter with support obtained by trapping the retrograde wire inside the antegrade guide catheter with antegrade balloon inflation.
3. Exchange of the retrograde wire with a RG3 wire, sometimes facilitated by trapping the micro-catheter.
4. RG3 wire tip is externalized through the hemostatic valve of the antegrade guide catheter.
5. The selected PCI device (e.g., balloon, stent) is inserted for delivery into the CTO lesion over the RG3 wire.

The performance of externalization is one of the most demanding techniques of retrograde PCI and the risk of complications among the highest. Several precautions need to be undertaken while doing this procedure (Tips and Techniques 15).

8.5. Vessel preparation and PCI

The ability to balloon dilate adequately via the antegrade approach may remain the final obstacle. Use of rota-ablation is controversial in this situation.

9. Complications encountered during retrograde PCI

Complication during this procedure may be similar to other PCI such as coronary perforations but many complications are unique to CTO PCI Table 4.

Perforation of collateral channel is one of the most dreaded complications while negotiating a collateral channel. If perforation is from septal collateral it may be self-limiting and may require nothing more than stopping the procedure although in some cases it may require coil embolization (from both ends). A perforation occurring in an epicardial artery is more consequential and may require pericardial tapping as well as distal occlusion of collateral by sub-cutaneous fat/thrombus or coil.

Channel ventricular fistula is another innocuous complication and requires nothing more than masterly inactivity.

Septal hematoma on the other hand is a dreaded complication which may cause severe pain in some cases but even more adverse consequences in others. The treatment involves:

1. Embolization of the septal channel.
2. Creation of fistula communicating with the ventricle.

Sub-intimal stenting is another complication somewhat unique to CTO PCI. The effects may not be apparent acutely but over long term may cause stent fracture, aneurysm formation or higher chances of restenosis.

Table 4
Complications unique to CTO PCI.

1.	Thrombosis and dissection of donor artery
2.	Perforation of the Collateral Channel
3.	Collateral Ventricular fistula
4.	Septal Hematoma
5.	Entrapment of PCI equipment in septal collaterals
6.	Sub-intimal stenting
7.	Radiation skin injury
8.	Contrast Induced Nephropathy

Tips and Techniques:

1. Procedural elements contributing to a successful and safe PCI

1. Optimal delineation of CTO segment, collateral vessel: location & course
   - Orthogonal views on cine angiogram
   - Contra-lateral injections
   - Use of MSCT
   - Use of IVUS before and during the procedure.
2. Calculation of maximal permitted contrast (6 × GFR in ml) and fluoroscopy time (60 min) prior to the procedure.
3. Availability and experience of using dedicated hardware
   - Guide catheters
   - Guidewires
   - Micro-catheters
   - IVUS
   - Other specialty hardware

2. How to perform contra-lateral injections

1. At low magnification
2. Prolonged imaging exposure
3. No table panning
4. First inject donor then occluded vessel to minimize radiation
5. Angiographic views
   - Septal collaterals may be best visualized – RAO cranial or straight RAO
   - Epicardial collaterals need specially tailored view
   - Distal lateral wall collaterals (OM-PLV, diagonal to diagonal/OM connections) – LAO & RAO cranial
   - Proximal OM and AV groove collaterals – RAO & AP caudal

3. How to save contrast

1. Use micro-catheters to give injections
2. Use contralateral route to give super-selective contrast injections delivered via micro-catheter embedded deep in collateral branch

4. When to stop

1. Collapse of true distal channel implying
   - large sub-intimal space is compromising distal true lumen
   - feeding collateral has got compromised
2. Adventitial staining – implying large sub-intimal space
3. Non visualization of feeding collaterals
4. Upper limits of radiation and contrast is exceeded
5. Any complication occurs
   - wire perforation
   - collateral perforation
   - septal hematoma
   - donor vessel compromise

5. Employing imaging techniques to identify course and characteristics of the occluded segment

1. Cine-angiogram (orthogonal views) – to identify proximal cap; dimple or flat stump – faint lumen inside CTO segment (existence of re-canalized lumen)
   - calcification or stent in the occluded segment
2. Contralateral injection
   - identify proximal and distal true lumen together
   - proximal and distal stumps moving out of phase with pulsation is a sign of tortuosity
3. CT angiography for 3-Dimensional appreciation
4. MSCT can visualize even angiographically invisible parts of occluded stump

6. When to use retrograde technique as the primary strategy

1. Failed antegrade attempt
2. Unknown antegrade entry point
3. Long CTO (>40 mm)
4. Heavy calcification or severe tortuosity within occluded stump
5. CTO within RCA bend point
6. Large side-branch within proximal cap
7. Antegrade guidewire makes huge sub-intimal space
8. Straight, big, visible septal collateral

7. Shaping of guidewire

1. Penetrating the proximal fibrous cap
   - Primary bend is made 1 mm from the tip and the angle should be shallow (<15°)
   - Secondary bend may bend may be given 4–8 mm from tip with a 10–15° bend which acts as a navigator to orient the tip.
2. Advancing wire within the occluded lumen
   - Primary bend is made 2–5 mm from the tip and the angle broad (45–90°)
3. Penetrating the distal fibrous cap - like proximal cap
4. Wire in true lumen – Primary bend is made 1–2 mm from the tip, wide angle (>60°)
5. Wire re-entering from sub-intimal space – large bend

8. Guidewire manipulations

1. Both hands maneuver – Left hand is used for to-and-fro movement and right hand used for rotation (quick and ~180° – drilling strategy; slow and <90° – penetrating strategy)
2. Only right hand maneuver – Right hand does both the movements; longitudinal and rotating while dissecting the tissue with wire tip

9. Location of entry point for penetrating fibrous cap

1. Tapered tip
2. Tactile location of 'dimple' – wire is carefully manipulated to achieve wire tip trapping towards a small hole (dimple)
3. IVUS location of dimple in a flat stump

10. Predisposing factors for sub-intimal penetration

1. Type of wire – hydrophilic or polymer coated (hydrophilic < polymer coated)
2. Eccentrically located stump of occlusion
3. Caput medusa
4. Use of micro-catheter or Venture catheter

11. Strategies to avoid sub-intimal passage

1. While negotiating bends keep the guidewire within the inner curve of the bend
2. If encountering resistance while forward movement
   - Pull back the wire to the point of proximal entry and then move in a different direction – Exchange with a stiffer wire
   - See-saw wiring using two micro-catheters
3. Orthogonal views to improve anatomic localization

12. Signs of true lumen entry

1. Distinct tactile feel – a feeling of dimple and crossing it
2. No resistance felt while moving wire back and forth
3. Free rotation of wire tip*
4. Retrograde injection reveals wire in true distal lumen on orthogonal views
5. Wire tip easily entering the side-branch

* Wire tip moving freely can be misleading because this can also happen with wire entering extra-vascular space.

13. Balloon inflation techniques to guide retrograde wire into distal true lumen

1. Double balloon inflation – simultaneous balloon inflation by two adequately sized balloons* in both antegrade and retrograde spaces to make these two spaces confluent. Once this happens retrograde wire can be directed through this channel into distal true lumen.
2. Retrograde balloon withdrawal – retrograde balloon is withdrawn while the retrograde wire is advanced, the maneuver getting the retrograde wire entry into antegrade space.

* It is important to choose size of the balloons carefully because too large a size can lead to rupture of the space.

14. Trapping the wires

1. Antegrade trapping – retrograde wire is trapped in the proximal lumen or the guide catheter allowing easy passage of retrograde micro-catheter / OTW balloon.
2. Retrograde trapping – trapping of antegrade wire (in antegrade crossing) by retrograde micro-catheter, allowing easy passage of balloon or stent into formerly occluded space.
3. Reverse trapping – retrograde wire is caught by antegrade snare.

15. Precautions to be undertaken while performing externalization and completion of the retrograde procedure

1. Avoid deep engagement of the donor guide – it can cause ostial dissection.
2. Protect the collateral channel from getting injured by the stiff guidewire by keeping a soft micro-catheter in the collateral especially at the4 time of withdrawal of retrograde assembly.
3. Withdraw soft end of guidewire from collateral channel synchronized with the heart beat.
4. Collateral angiogram in orthogonal views should be performed both after removal of micro-catheter from channel and removal of the wire.

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