The Editor acknowledges all the Authors that kindly shared their enthusiastic efforts to the accomplishment of this work, alongside all the institutional teams and participants that helped to gather the whole amount of information presented in this narrowly focused therapeutic field.
In the early 70’s I had the opportunity to participate with Dr. Edward Garret and Dr. Michael DeBakey in Houston, Texas in the first reported procedure involving a reversed autogenous saphenous vein graft from the common femoral artery to the dorsalis pedis artery in a patient with severe infrapopliteal arterial occlusive disease. The success of the operation, at that time, established a gold standard for treatment of that particular vascular pathology. It might well have been christened “straight line” foot revascularization. And indeed, for decades the presence of a palpable dorsalis pedal pulse or even the more sensitive Doppler evaluation at the anastomotic level, gave proof of at least the potential for foot viability.

Fast-forward four decades. It should not be enlightening to recognize that the enormous evolution of endovascular therapy has precipitated a volcanic change almost beyond measurement. Only a glimpse at any current worldwide program on critical limb ischemia demonstrates a preponderance of atherectomy, thrombectomy, stents including the drug eluding and biodegradable, cryoplasty, genes and beyond. Observing such a potpourri of proposed therapeutic remedies must evoke a cerebral pause. “More” is often not better but only a temporal remedy - a “straight line” waiting for a better solution.

The reader of this enormously important contribution will certainly be intrigued by the potential for that better solution. Dr. Alexandrescu introduces in CLI applications the angiosome model (AM) concept of perfusion-targeted angioplasty, the key to feeding arterial flow to the site of ulceration, in descriptive detail. In doing so, establishes the foundation for his distinguished contributors to expand across the field of critical limb ischemia with special focus on subjects like reperfusion, neuro-ischemic wounds and collateral reserve.

While lesion directed flow revascularization, rather than a “straight line” unspecified foot revascularization, has already achieved wide success, as the contributors point out, AM targeted angioplasty presents significant technical challenges since the aim is reconstitution of the obstructed, more difficult vessels in contrast to those more visible, larger, pliable and accessible approached in common practice. Moreover, although technology has evolved, new challenges in engineering, drug and pharmacologic research, gene and nanotechnologies as well as others will be required. As in all of our research endeavors, we must view our corporate colleagues as partners.

Predictably, with more durable efficacy being the continuum of this exciting scientific pathway as portrayed in the second chapter by Dr. F. Serino, the pendulum will swing from heroic limb salvaging revascularization, to defined and planned more preemptive interventions for wound healing.

This scientific contribution is a major influence on that pendulum shift.

Edward B. Diethrich
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HISTORICAL AND ANATOMICAL CONSIDERATIONS

The angiosome model of perfusion (AP) essentially relies on the anatomical studies published by Taylor et al. since 1987 and further developed by Attinger et al., in the plastic reconstructive surgery field. These authors described a three-dimensional perfusion model of the human body following specific arterio-venous bundles that allow preferential strategies for tissue reconstruction, surgical access and revascularization.

The important role of territorial arterial distribution and appended collateral supply in humans was already stipulated among others, by Matas in his pioneering publication at the beginning of the last century. The human body holds a vast network of arterial and venous interconnections dependent of the main peripheral vascular axes. Regarding this arrangement from a “fractal” point of view (repetitive patterns for irritation), a few staged levels of arterio-venous graded flow could be individualized.

Focusing on the inferior limb perfusion, it could be then described: a genuine Level I distribution, containing the original iliac and common femoral arterial and appended venous axes, the Level II of dichotomy, gathering the superficial and profunda femoris arteries and the three tibial trunks, further Level III of division, featuring specific ramifications addressing peculiar zones of tissue in the limb, Level IV of perfusion, that holds large to small size collaterals (also called “choke-vessels”), the next Level V represented by the arterioles, and finally the Level VI assembling the capillary network.

Promoting similar topographical points of view in a regionally-based evaluation, the anatomical studies of Taylor and Attinger specifically develop the «Angiosome concept» and demonstrate distinct 3-dimensional tissue sectors of vascularization in the human body fed by peculiar arterio-venous bundles. These sectors named “the angiosomes”, assimilate equivalent “arteriosomes” and correspondent “venosomes” that nourish their characteristic 3-D tissue containers. Adjacent angiosomes are linked by numerous communicants the “choke vessels”. These interconnections between neighboring angiosomes create an effective compensatory system against any hostile hemodynamic condition and seem particularly operative in non-atherosclerotic limbs. The «angiosomes» adding the «choke vessels system» may be assimilated to Levels III and IV in the fractal model of perfusion evoked above, respectively.

Revascularizations performed more distally in the leg, beyond Level II of segmental perfusion may be of great value in critical limb ischemia (CLI) treatment, particularly while following the topographical distribution of ischemic injuries. In subjects exhibiting massive «choke-vessels» (Level IV) depletion, alike those suffering from diabetic arteriopathy, the Buerger disease or end-stage renal disease (ESRD) syndrome, the angiosome concept may offer new insights in planning targeted tissue recovery revascularization.

SUCCINCT ILLUSTRATION OF THE FOOT AND ANKLE ANGIOSOMES

Considering the lower leg vascular anatomy, the previously described “angiosomes” of the foot...
ANGIOSOMES APPLICATIONS IN CRITICAL LIMB ISCHEMIA

and ankle include the following groups (Figure 1.1):

a. the medial calcaneal, the medial plantar and lateral plantar arteries angiosomes derived from the posterior tibial artery, supplying the entire plantar heel and the medial and lateral plantar surface beyond the toes;

b. the dorsalis pedis angiosome, which prolongs the anterior tibial artery, nourishing the dorsal area of the foot and the toes, also ensuring the upper anterior peri-malleolar vascularization;

c. the lateral calcaneal artery angiosome derived from the peroneal artery covering the lateral and plantar heel. At the upper ankle level, the anterior peroneal perforating branch angiosome, equally originates from the peroneal flow and connects the peroneal to the anterior tibial territory;

d. as going up to the superior ankle, other angiosome and appended territories were described, such as: the antero-lateral malleolar with its cor-
Figure 1.2 and figure 1.3 illustrate several examples of ischemic foot wounds before and after specific dominant angiosome revascularization.

**NATIVE CONNECTIONS BETWEEN DIFFERENT ANGIOSONES OF THE FOOT AND THEIR PRACTICAL IMPLICATIONS IN REVASCULARIZATION**

A high number of arterial anastomoses have been described as to supply neighboring foot and ankle angiosomes. However, it is beyond the purpose of this chapter to thoroughly detail these anatomical details, much better described in previously dedicated studies. The arterial communicants between different leg angiosomes encompass a large variety of collaterals, conventionally classified from “small” to “large”, incorporated in the Level IV of sequential perfusion evoked above. Some of these “large” and “medium-sized” tibial and foot collaterals, the “first-line” or “rescue” communicants (belonging to the Level IV of perfusion), seem to play a particularly important role in initial phases of secondary flow redistribution in CLI, additionally to the vast “choke vessels” system (“small size” Level IV collaterals). These “rescue” communicants may assume a pivotal role in regional foot reperfusion particularly after direct (AP-oriented), however more frequently in the common practice after indirect (AP-independent) revascularization. Regardless of the type of flow reconstruction (direct vs. indirect), the ensuing groups of “rescue” communicants with critical role in ischemic tissue regeneration, can be summarized as follows:

- regarding ischemic heel ulcers: the connections between the posterior tibial and peroneal arteries (via the medial and lateral calcaneal branches of both arteries, also via the peroneal posterior communicant branch) play an important role in related peri-calcaneal vascular reconstitution;
- regarding forefoot and toes ischemic tissue defects: the communications between the anterior (dorsalis pedis) and the posterior tibial (plantar) arteries either directly, at the level of the first metatarsal interspace, or via matched metatarsal collateral irrigation (through paired anterior and posterior digital collaterals from both arches origin), play a substantial role in tarsal/metatarsal reperfusion;
- concerning the peri-malleolar and postero-lateral ankle wounds: the lateral peri-malleolar anastomoses linking the peroneal (via the anterior perforating branch) with the anterior tibi-
al (via the antero-lateral malleolar branch), together with the medial peri-malleolar network (via corresponding medial malleolar branches from both, the anterior and posterior tibial arteries), represent distinct alternatives for local blood supply in the ankle, for CLI tissue defects;

- applying to the plantar ischemic wounds (currently more extended than common “bare neuropathic perforating ulcers” of the diabetic foot); the communicants from both plantar arteries (medial and lateral, both arising from the posterior tibial artery) are linked to the lateral and medial tarsal arteries (via the anterior tibial artery) and represent notable deviations for compensatory irrigation to the ischemic sole.

According to recent studies, specific CLI presentations concerning the “diabetic foot syndrome” and the “renal patients” seem to cast particular barriers in foot flow redistribution since indirect revascularization (without angiosome orientation) is performed. Indeed, compared to common “bare atherosclerotic” CLI subjects, patients exhibiting long-lasting diabetes mellitus or ESRD add severe depletion in all categories of foot collaterals (Level IV) and seem to be particularly prone to incomplete ulcer healing.

It has been suggested that the neuroischemic “diabetic foot syndrome” mainly issues from the more distal and aggressive “atherosclerotic macroangiopathy” typically located in the tibial trunks and the functional microcirculatory impairment induced by both neuropathy and local sepsis. Owing to these multiple occlusions in the large and medium-sized foot collaterals (the “rescue” communicants contained in the Level IV of perfusion), O’Neal concluded that this “end-artery occlusive disease” could have notable implications for the choice of revascularization (direct vs. indirect). The novel “end-artery disease” theory distinguishing the “diabetic foot syndrome” may highlight why the AP concept and related direct revascularization, may offer better hemodynamic conditions for ulcer healing in diabetics and more widely, in all collateral-deprived patients.

**PREDICTABLE PHASES OF FLOW REDISTRIBUTION AFTER CLI REvascularization**

As equally evoked further in chapters V and VIII, it becomes more explicit in many author’s opinion that even providing the best flow via indirect revascularization through preserved and suitable collateral patterns, the newly enhanced flow will afford only limited compensatory capacities, more precisely less than 40% of the initial perfusion (before CLI initiation) or by comparison to equivalent direct arterial reconstruction.

Regardless of the type of revascularization, there were described three phases of flow redistribution following critical ischemic tissue reperfusion: a. the initiatory flow redistribution, concomitant with the revascularization technique, best assessed by current peri-procedural angiography, the wound-related “angiographic blush”, or by the novel “indocyanine green” angiography technique. This phase mainly concerns specific angiosome-related branches (Level III), the foot arches (Level III), and the remnant “rescue” collaterals (“large” and “medium sized” collaterals or, Level IV of fractal perfusion);

b. the early or mid-term flow dispensation (30 min to 50 min after reperfusion), regarding the remnant “small collaterals” (Level IV of perfusion) or “choke vessels”. A few methods were proposed as to enable the interventionist to ascertain the characteristics of this early postoperative reperfusion, although each of them showing specific advantages and inherent drawbacks (see also Chapters II and VIII). Some of these diagnostic tests appear to pro-
vide encouraging results, alike the trans-cutaneous sensi-laser system (SPP), equally further detailed in this volume (Chapters II, V, and VIII); c. the retarded hemodynamic changes (several days or weeks after the initial procedure), essentially concerning the local arteriogenesis and angiogenesis processes, or Levels V and VI of perfusion, respectively. New diagnostic methods that focus on the specific assessment of “regional perfusion” (Levels III to VI) before and after CLI revascularization, such as the PET scan, foot scintigraphy, capillaroscopy and the mass spectrometry devices may prove real utility in this setting in the future.

**SCORING THE COLLATERAL ARTERIES THAT INTERCONNECT THE FOOT ANGIOSOMES**

As stated in the first paragraph, the angiosome theory was initially illustrated in ex-vivo models.

Beyond a few possible 6% up to 9% individual anatomical variations concerning the tibial or the foot arteries distribution, the same six angiosomes of the foot and lower ankle were described in general population without particular ethnic alterations. The only variable explaining individual differences in the extent of each leg angiosome, seems to be dictated by the amount of lasting collaterals that interconnect these vascular territories.

Some specific CLI conditions strongly influence the fate of these “rescue” collaterals or that of the “choke vessels” (Level IV of perfusion), and are further discussed in Chapter VIII.

By practical reasons, a few principal risk factors for collateral depletion (Level IV), but also for impaired arteriogenesis and angiogenesis (Levels V, and VI) documented in the contemporary literature are summarized in Table 1-I.

A correlated “collateral risk score” estimation (n /10 points) with practical value in our institution is additionally reproduced (Table 1-I):

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt;70 years</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Diabetes &gt;10 years</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>ESRD</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Severe Neuropathy (g 5-9/ UK Score)</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Previous Amputation &amp; Ulcer</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Thrombophilia</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Foot Abscesses</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Heel &amp; Hind foot Ulcer</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Extended Foot Ulcer &gt;1.5 cm</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>LV Ejection Fraction &lt;30%</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Initiatory depletion</td>
<td>0-2 P/10 P (Total 10 P)</td>
<td></td>
</tr>
<tr>
<td>Moderate depletion</td>
<td>3-4 P/10 P (Total 10 P)</td>
<td></td>
</tr>
<tr>
<td>Severe depletion</td>
<td>&gt;4 P/10 P (Total 10 P)</td>
<td></td>
</tr>
</tbody>
</table>

Ischemic ulcers in patients exhibiting moderate or severe collateral deprivation (Table 1-I)
may particularly benefit from specific angiosome-guided revascularization by applying the “first choice”, or direct (AP-oriented) arterial reconstruction (Table 1-II).

**THE CHOICE OF THE MOST ADAPTED ANGIOsome THAT FITS THE FOOT WOUND’S TOPOGRAPHY**

The incorporation of the AP concept in current vascular practice may shift «classical» indications from «which vessel is most accessible for revascularization» to a multidisciplinary clinical perspective: «which region of perfusion regulated by which artery should be treated, according to each wound location? ».

The angiosome strategy essentially delineated a clinical mode of reasoning in the decision-making algorithm of BTK targeted revascularization. The wound topography becomes the first step in planning and achieving selective tibial and foot arteries reperfusion, before acknowledging arteriographic details (the second stage in this proceeding).

Knowing that up to 70% of foot ischemic wounds may have single dominant angiosome affection, careful assessment of the wound topography at the time of the first debridement is mandatory. In our team’s current practice we have adopted a schematic algorithm that may enable distinct therapeutic choices when planning intervention (Table 1-II). Following each ulcer’s locations and according to the foot angiosomes allotment, all available arteriographic features are thoroughly depicted for every given presentation. The vascular interventionist is then confronted with several alternatives while foreseeing the best treatment to cast (Table 1-II): the “first choice revascularization” represented by direct (AP-guided) arterial reconstruction, if technically feasible, also taking into account the “second” and optionally the “third” compulsory choices for indirect (AP-indifferent) revascularization, in cases when the initial approach may fail.

In the same Table 1-II, are also depicted possible “tandem angiosomes” indications in revascularization, concerning the remnant 30% of more complex ischemic presentations encountered in the current practice, that engage larger tissue defects from neighboring angiosomes hypoperfusion.

**ANATOMICAL CONSIDERATIONS AND SPECIFIC FEATURES OF THE ISCHEMIC WOUNDS**

Beyond precise ulcer location and consequent flow dependency evaluation, a meticulous codification of each wound characteristics is necessary.

A thorough stratification of each tissue defect including the extent, the depth, the percentage of surrounding viable tissue in the foot and specific associated risk factors (such as infection, neuropathy, low albuminemia, renal insufficiency, metabolic or autoimmune disorders, thrombophilia, etc.) is equally required. Tissue defects should be explicitly classified following the Rutherford ischemic stratification and by other corresponding “diabetic foot” scoring systems, with realistic recovery expectations expressed in multidisciplinary common consent.

**POSSIBLE NEW ALGORITHM FOR REVASCULARIZATION FOLLOWING ANATOMICAL ALLOCATION OF ANGIOsOMES IN CLI FOOT WOUNDS**

As succinctly evoked in the previous paragraph, there are undoubtedly some important steps to take in planning AP-guided revascularization for ischemic foot wounds. They could be briefly listed as follows:

1. allow careful clinical evaluation of wound location related to the previously described angiosome’s distribution in the foot and ankle (schematically depicted in Figure 1.1. The features of each ulcer and its inflammatory extent should be precisely appreciated and scored upon available classification systems. It has been stipulated that 75-80% of the lower extremity tissue defects globally encompass the heel, the sole with plantar side of the toes and the dorsum of the foot.
In these presentations, the vascular interventionist could gather important information concerning the dominant ischemic angiosome to be treated upon attentive analysis of wound topography. For more challenging situations involving extended forefoot, or global hind foot and plantar ischemic wounds, tandem arterial axes may be mandatory to consider for revascularization, if technically feasible.

2. Provide detailed vascular iconography of the affected foot territory and correspondent contralateral limb arterial perfusion:

a. if the vascular interventionist has the choice for deliberate opening of one or more BTK vessels, or if two vessels are mandatory to be reperfused, a first attempt in the specific wound-related angiosome artery (direct revascularization) (Figures 1.1-1.3) is recommended. For ulcers that exceed 1.5 cm in diameter, tandem angiosomes affection could be suspected: for those being located in the heel, both posterior tibial and peroneal arteries should be targeted; for forefoot and toes wounds >1.5 cm, a safer tandem anterior tibial (through the dorsalis pedis angiosome) and posterior tibial artery reperfusion (via the lateral and medial plantar arteries) might be serviceable; if all calf vessels are occluded and the AP-dependent artery cannot be reopened, an alternative arterial source ("second", or "third-choice" angiosome - Table 1-II) might be planned. The interventionist should be however aware of predictable failure hazard in the healing process by using these compulsory indirect alternatives for revascularization. As it has been evoked in parallel contemporary analysis, these "rescue" solutions are essentially based on the meager 30-40% indirect reperfusion, still available via some scarce remnant collaterals.

b. if all calf vessels are occluded and the AP-dependent artery can be successfully reopened, the interventionist should seek for simultaneous distal run-off reperfusion according the original AP strategy. The endovascular techniques may allow synchronous treatment in adjacent calf and foot arterial axes. For dorsal foot wounds, the dorsalis pedis angiosome (from the anterior tibial artery) needs to be focused first; for plantar ulcers, the medial or lateral plantar arteries angiosomes (from the posterior tibial artery) ideally should be considered for targeted revascularization. For small ulcers (less or equal to 1.5 cm) of the internal or external heel, alternatively the posterior tibial (through the medial calcaneal angiosome), or the peroneal artery (via the lateral calcaneal angiosome) need to be privileged. For isolated lateral ankle trophic defects, the peroneal artery may be selected for specific reperfusion (through the lateral calcaneal and postero-lateral malleolar angiosomes).

c. If all the calf vessels are occluded and the AP-dependent artery cannot be reopened, an alternative arterial source ("second", or "third-choice" angiosome - Table 1-II) might be planned. The interventionist should be however aware of predictable failure hazard in the healing process by using these compulsory indirect alternatives for revascularization. As it has been evoked in parallel contemporary analysis, these "rescue" solutions are essentially based on the meager 30-40% indirect reperfusion, still available via some scarce remnant collaterals.

3. Assess the remnant collateral reserve and the dominant foot arch that still remains permeable. Beyond their critical number, caliber and appended interconnections, the remnant collateral network dramatically influences the fate of indirect revascularization. Diabetes mellitus and ESRD are two reputed pathologies as to enhance peculiar large and medium-size collateral depletion and diminished arterio- and angiogenesis (Levels IV to VI) in the CLI affected leg.

By comparing bilateral CT or MR-angiograms, the interventionist may also be aware of eventual anatomical anomalies in calf and foot vessels. He or she may then focus revascularization upon the dominant foot arch perfusion and dependent collateral path. More precisely (Figure 1.1-1.3) concerning the heel ulcers, if the posterior tibial artery cannot be reperfused, the peroneal artery may assume the "second choice" for indirect revascularization, although strongly conditioned by good caliber communicating branches in the posterior ankle and hindfoot. For plantar wounds, if the plantar arteries are unattainable neither by antegrade (via the posterior tibial artery), nor by retrograde way (owning the "loop" technique
and via the pedal access), the medial, the lateral tarsal arteries, or the first metatarsal perforating branch (from the dorsalis pedis angiosome) may represent “second compulsory options” for revascularization. Finally concerning the hallux, the toes and a majority of forefoot tissue defects, despite unachievable posterior tibial (or alternatively dorsalis pedis reperfusion), by following the local dominant arch pattern, flow compensation can be achieved via the first metatarsal artery and his perforating branch from both, the dorsalis pedis or the plantar network.

Complementary anatomical references about the angiosome distribution and appended clinical implications in wound healing are further undertaken in Chapters II, III, VI-VIII. Other connotations focusing each angiosome's topography, connections and particularities for access and reperfusion will be available in chapters III-V, VII and VIII, as well.

REFERENCES