"Practical application" of leucocyte- and platelet-rich fibrin in wound care:

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Important aspects to consider during a first treatment:

1. Start by cleaning the wound, first with a wound shower using a physiological solution and then, depending on the "needs of the wound", with a wound cleanser (e.g., Prontosan ®, Flamirins ®, or Vashe ®), or by soaking a compress with the cleanser and leaving it in contact for 5 to 10 minutes, according to the product's instructions.
2. Disinfect the surrounding skin with a non-cytotoxic broad-spectrum antiseptic (e.g., Isobetadine ®). Respect a contact time of at least 1 minute.
3. Perform a curettage to remove necrotic material, sloughed tissue, crusts, and/or microbial material from the wound, including wound tunnels or cavities, and wound borders to promote wound healing. Try to activate the wound surface by creating small bleeding points. Excise avital, atonic deflecting wound edges. A deep and extensive curettage must be avoided after the first treatment.
4. Protect the wound edge and surrounding area to prevent skin maceration, especially in cases of heavily exudating wounds. You can eventually apply a protective spray to the wound periphery (e.g., Cavilon ® spray), to prevent maceration. If the surrounding skin is very dry, apply a topical moisturizing oil (e.g., Linovera ®), taking care to only apply it to the surrounding skin and not to the wound bed.
5. Inject small drops of L-PRF exudate (rich in growth factors and with antiseptic activity) into the wound periphery and, if possible into the wound itself. Use a fine needle (30 to 33 gauge). These injections will stimulate tissue angiogenesis into the wound, enhance the antibacterial effect, and promote tissue regeneration in this region. The exudate injection points will also generate bleeding points.
6. Apply L-PRF membranes from the periphery to the centre. If the wound cannot be completely covered with a layer of membranes, spaces can be left between the membranes, and their position alternated in the following treatment. When using clots, apply in situ compression to the entire wound area with a gauze to remove excess exudate. Place the "face" part of the membranes or clots where most support for healing is needed.
7. Cover the wound area, membranes and wound edges (at least 2 cm) with a perforated **"primary"** dressing with silicone coating (e.g., Adaptic touch ® or Mepitel One ®), or a paraffin gauze dressing like Leukoplast Cuticell Classic ®, Jelonet ®. The silicone layer or paraffin gauze prevents adhesion to the L-PRF membranes and ensures that the membranes remain wet; desiccation of the membranes must be prevented at all times to promote and enable their biological action. When using a paraffin gauze, a Tegaderm film ® must be applied over the paraffin gauze to seal the wound and keep it moist.

This primary dressing also stabilises the membranes during the first 48 hours, allowing the secondary dressing to be changed without altering the action of the membranes. Absorbent dressing or gauze should never be placed in direct contact with the membranes.

8. Apply a non-woven (e.g. Mesoft ®) or absorbent compress to absorb the wound fluid. This **"secondary"** dressing can be replaced whenever needed without manipulating the underlying primary dressing, thus avoiding the disruption of the wound healing process. For deeper wounds, if the wound cannot be filled completely to the level of the wound edge with L-PRF membranes, cover the membranes with a non-adherent material and then fill the remaining space with compresses to ensure a stable covering of the L-PRF membranes.
9. Finally, a **"third layer"** must be applied (e.g., an adhesive bandage (e.g. Mefix ®) or an elastic gauze bandage to secure the other dressings and to protect the wound.
10. Provide the patient with a letter explaining the treatment (e.g., stating that the secondary dressing may be replaced, but the primary (contact layer) must remain untouched.
11. In the case of a venous ulcer, it is extremely important to maintain compression therapy as indicated by the treating physician.
12. The patient should also receive information about potential alarm signals that require contacting the healthcare provider (e.g., significantly increased exudate, strong odour, pain, fever, itching).

9." As an alternative to the aforementioned method (contact layer + secondary dressing + fixation), a self-adhesive foam dressing with a silicone contact layer can be chosen (e.g., Mepilex Border ®). This dressing will provide greater comfort for the patient and optimally maintain the moist wound environment. However, its application is only indicated for low-exudate wounds, as this dressing must remain completely undisturbed for 7 days to ensure the best possible fixation of the membranes. Additionally, the wound location must be suitable for the use of a self-adhesive foam dressing.

9."' In case of exposed bone where the periosteum is no longer present, the silicone contact layer can be replaced with a traditional wound contact layer (paraffin-impregnated gauze) to achieve a slightly more moist/greasy covering.

Points of attention for 2nd and subsequent treatments (weekly).

1. Clean the wound (see above).
2. Check the L-PRF membranes. The membranes that are attached and integrated to the wound surface or that have already partly transformed into granulation tissue should not be removed!
3. Loose or dry L-PRF membranes, necrotic tissue, sloughed tissue, biofilm and crusts have to be removed.
4. Repeat steps 4 to 9 (see above), but avoid deep curettage.
5. Repeat this procedure weekly until the wound is completely covered with healthy epithelium. At the end of treatment, longer time intervals (e.g., two weeks) may be considered.

The need for painkillers should decrease significantly after the first applications of the L-PRF membranes, and the unpleasant odour of the wound should be replaced by the typical odour of using L-PRF.

Aftercare:

- Inform the patient about the importance of the correct medication/measures to prevent recurrence!
- The treated wound must be cared for with a moisturising skin ointment and protected from direct sun exposure (use sunscreen) or injuries!
- Provide the patient with a letter explaining the treatment (e.g., stating that the secondary dressing may be replaced, but the primary (contact layer) must remain untouched).
- The patient should also receive information about potential alarm signals that require contacting the healthcare provider (e.g., significantly increased exudate, strong odour, pain, fever, itching).

Contra-indications for the use of L-PRF:

- when causal and sustaining factors are not or insufficiently treated, or when necessary, preventive measures are not implemented (the therapy will then be less successful),
- in cases of atypical and special (dermatological) ulcers: pyoderma gangrenosum, calciphylaxis cutis, etc.;
- in patients with active oncological therapy,
- in wounds containing malignant tissue (oncological ulcer); however, oncological wounds, where the malignant tissue has been removed, are eligible,
- in the presence of “untreated osteomyelitis” related to the wound (if no targeted antibiotic therapy has been initiated),

Points of interest:

- limited therapy adherence and basic hygiene require extra follow-up and education,
- deep or large wounds can be more demanding because of the stability/proper fixation of the membranes; the latter requires special attention,
- the same applies to wounds with high exudate levels which may jeopardize membrane stability
- using anticoagulants is not a contraindication for L-PRF application, and stopping anticoagulants is not indicated.
- compression therapy, when needed, can be combined with L-PRF treatment.
- take precautions if the wound is in areas at risk of contamination (e.g. around the anus or in the genital area or in the sacral area in patients without sphincter control); use appropriate dressings and indicate that the dressing should be changed in case of contamination; if dirt has reached the primary dressing, the patient should go to the health care provider for cleaning as soon as possible.

Peri-wound irritation or an increased microbial load:

Peri-wound irritation without suspicion of a bacterial/fungal component, will be treated with skin protectors. Skin protection is provided or not, based on the expected amount of exudate and the skin condition. For this purpose, a barrier film or spray is used, which is applied to the wound edges and the peri-wound area. In case of doubt about the necessity, skin protection is always chosen. Severe peri-wound irritations can lead to the discontinuation of L-PRF therapy. In cases of irritation or itching attributable to an allergy to any of the dressings, change the dressing to an alternative. Consider applying a topical antihistamine or corticosteroid (e.g. Clobetasol Propionate ®) locally and only if necessary.

In the case of a precarious skin condition or signs of **maceration**, skin protection is certainly indicated and the application of an elastomer skin protector can even be considered (unless there is a suspicion of fungal load or critically increased bacterial load). The use of creams, ointments, pastes, or lotions is contraindicated as they hinder the fixation of the L-PRF membranes. However, in case of a very dry skin with irritation, one can use an oil (e.g., called Linovera ® or Clobetasol Propionate ®); but to ensure the fixation of the dressings, one should use elastic gauze bandages, which do not require adhesion. The use of topical antibiotics on the peri-wound area is also contraindicated, even in the presence of signs of peri-wound infection.

If **maceration** and/or irritation cannot be controlled with this, L-PRF therapy is temporarily halted and replaced for 5 to 7 days with an antiseptic therapy of the wound with a broad-spectrum antiseptic (e.g., Isobetadine ® once a day).

In case of signs of **increased microbial load** at the wound and/or peri-wound, the severity (Figure 1) and the suspicion of reversibility must be assessed by the healthcare provider.

(a) In cases of contamination and colonization, there are no points of attention, and the therapy is continued.

(b) In cases of classic local infection, L-PRF therapy is temporarily halted and replaced for 5 to 7 days with a high-antiseptic topical therapy using a broad-spectrum antiseptic (e.g., Isobetadine ® twice a day).

(b) In cases of spreading or systemic infection, L-PRF therapy must be stopped immediately for a longer period.

The duration of the antiseptic treatment should be extended by 1 week from the disappearance of clinical signs of infection in case of a fungal load. In cases of subtle local infection, the signs of infection may be reversible with a single thorough cleaning and disinfection, after which L-PRF therapy is resumed. However, subtle infection should

be considered as a spectrum. Within this spectrum, the healthcare provider can assess whether the degree of microbial load leans more towards colonization or classic infection, or vice versa. In other words, the healthcare provider assesses the severity and the suspicion of reversibility of the subtle signs of infection. In case of doubt, the therapy is temporarily halted, just like with classic infection. It is not recommended to perform L-PRF therapy more frequently than once a week in case of increasing signs of infection. In that case, stopping the therapy is the only responsible choice.

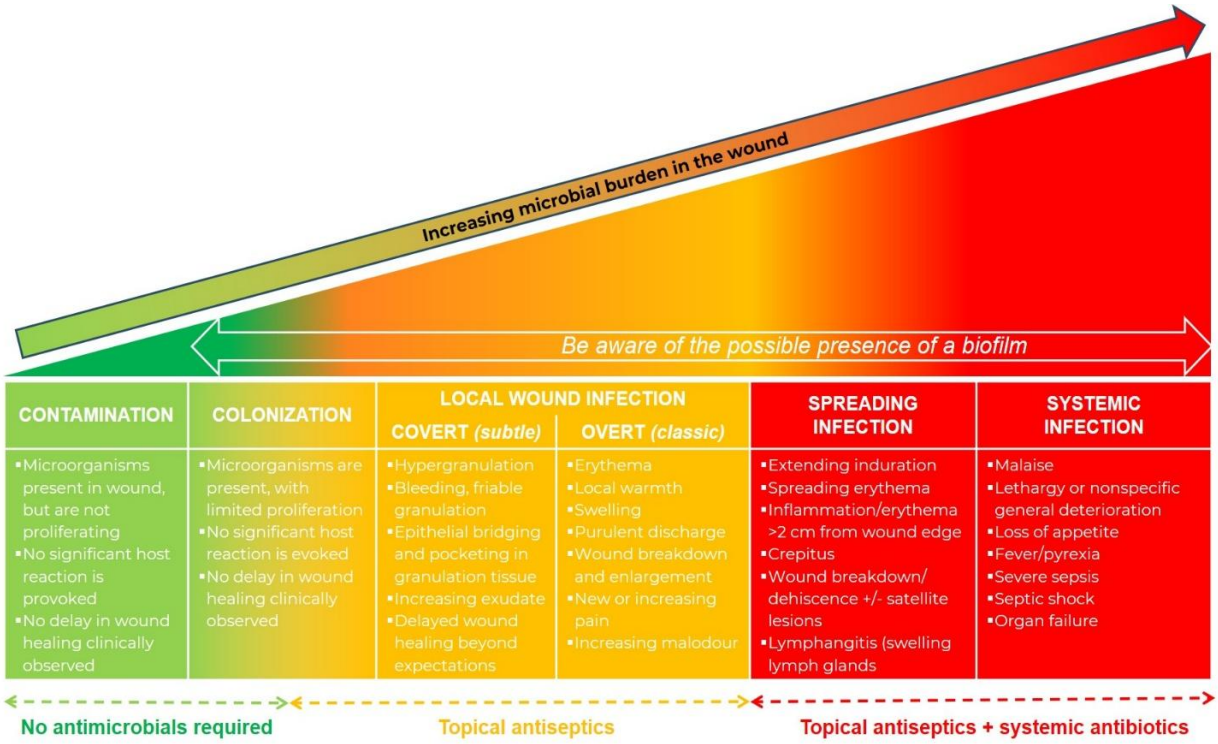

Figure 1. Adapted from: International Wound Infection Institute (IWII). Wound Infection in Clinical Practice. Wounds International. 2022.