A biofilm based wound care pathway in the community setting: a review

KEY WORDS
- Antimicrobial
- Biofilm
- Biofilm based wound care
- Debridement
- Monofilament pad

In recent years, the impact of biofilms on non-healing wounds has gained increasing interest and it has been reported that between 80% to 100% of non-healing wounds have a biofilm associated with them that impedes wound healing (Bjarnsholt et al, 2017; Malone et al, 2017). Biofilms consist of a complex community of microorganisms, which tend to attach to surfaces, and are encased within a matrix consisting of extracellular polymeric substances (EPS) (Malone et al, 2017). This matrix provides the microorganisms with protection against antimicrobial treatment and an individual's immune system. There is an increasing focus and awareness around the use of biofilm based wound care (BBWC) pathways, and they are recommended in several consensus documents (Bianchi et al, 2016; Shultz et al, 2017; Murphy et al, 2020; International Wound Infection Institute (IWII), 2022), This article will discuss the evidence behind BBWC and the potential for introduction of a BBWC pathway into the community setting.

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In 2008, the publication of several seminal studies (Bjarnsholt et al, 2008; James et al, 2008; Wolcott and Rhoads, 2008) began, among others, to look at the presence, identification and impact of biofilms on non-healing wounds and the implications of this for wound management practice. In the years since, the impact of biofilms on non-healing wounds has gained increasing interest and it has been reported that between 80% to 100% of non-healing wounds have a biofilm associated with them that impedes wound healing (Bjarnsholt et al, 2017; Malone et al, 2017). Biofilms consist of a complex community of microorganisms, which tend to attach to surfaces, and are encased within a matrix consisting of extracellular polymeric substances (EPS) (Malone et al, 2017). This matrix provides the microorganisms with protection against antimicrobial treatment and an individual's immune system. This allows them to withstand nutrient and moisture deprivation and changes in pH level and can also contribute to a low localised oxygen tension, further delaying wound healing (James et al, 2008; Metcalf, Bowler and Hurlow, 2014; Percival et al, 2015; International Wound Infection Institute (IWII), 2022). Biofilms can also increase the risk of repeated full clinical infection developing (Metcalf and Bowler, 2013; Bjarnsholt et al, 2017) and significantly delay wound healing by prolonging the inflammatory response and physically impeding the progression of granulation tissue and epithelial cells (World Union of Wound Healing Societies (WUWHS), 2016; Wolcott, 2017). There is currently no gold standard to identify biofilm presence (IWII, 2022). Despite this, due to their recognised prevalence within non-healing wounds, it is vital that clear and effective management strategies are put into place. The annual reported NHS cost of wound management in 2017/2018 was £8.3 billion, with 81% of this cost incurred in the community setting (Guest et al, 2020). In recent years there has been an increasing focus and awareness around the use of biofilm based wound care (BBWC) pathways. This article will discuss the evidence behind BBWC and the potential for introduction of a BBWC pathway into the community setting, where treatment of chronic non-healing wounds makes up a large part of the community nurses' caseload.

Biofilm based wound care pathways

In a non-healing wound a full wound assessment should be completed and the identified issues addressed, and if healing does not then resume, it is

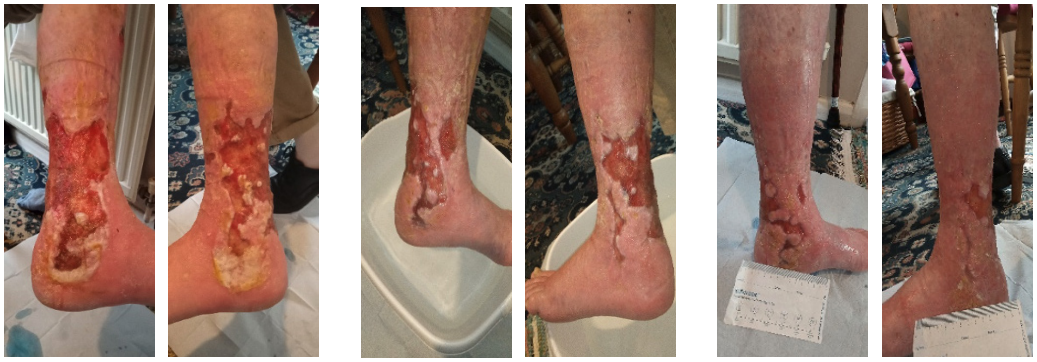
advised to consider the presence of a biofilm (Bianchi et al, 2016; IWII, 2022). Treatment should include vigorous cleansing and regular debridement followed by topical antimicrobial treatments, excluding topical antibiotics (WUWHS, 2016; Shultz et 2017; Wounds UK, 2017; Murphy et al, 2020; IWII, 2022). BBWC pathways are recommended in several consensus documents (Bianchi et al, 2016; Shultz et al, 2017; Murphy et al, 2020; IWII, 2022), however anecdotally, within the community setting, BBWC is not widely recognised or put into practice, and in some areas locally, there are currently no BBWC pathways in place. Shultz et al (2017) recommend 'the most effective debridement alongside the most effective antibiofilm treatment' and Murphy et al (2020) elaborate on this by recommending a 4-stage treatment strategy including cleansing, debriding, refashioning wound edges and antimicrobial/antibiofilm dressings. The consideration and introduction of a BBWC pathway to the community setting, to be used alongside clinical judgement, is therefore crucial considering the potential prevalence and resistance of a biofilm and its subsequent detrimental impact on wound healing.

The importance of debridement

In 2010, an *in vitro* study, carried out by Wolcott et al, hypothesised that newly formed biofilms are more susceptible to antimicrobial treatment. Thus demonstrating the importance of regular effective debridement to BBWC, with the aim of preventing the persistence and regrowth of antibiotic tolerant biofilms. The study used three separate *in vitro* models to investigate biofilm susceptibility to antimicrobials. In all models it was shown that, within the first 24 hours, the biofilm suspensions being created, using either *Staphylococcus aureus* or *Pseudomonas aeruginosa*, were more susceptible to the selected antibiotic (gentamycin). Furthermore, they became increasingly tolerant after maturing for up to 48 hours (p=0.05). In all biofilm models, *Pseudomonas aeruginosa* was completely resistant to gentamycin within 48 hours and *Staphylococcus aureus* within 96 hours. There were no significant differences detected between CFU (colony forming unit) counts of control biofilms and gentamicin treated biofilms. Alongside this, Walcott et al (2010) also carried out a small clinical study (n=3) on venous leg ulcers (VLU) that all had significant levels of *Pseudomonas aeruginosa* (average: $5.2x10^8$ CFU/5mg bioburden). At 24 hours post sharp debridement, sensitivity to antibiotic (gentamycin) treatment was significant, showing greater than a nine-fold reduction in concentration in relation to the control biofilm. At 48 hours two of the debridements still showed higher sensitivity to antibiotics and at 72 hours the biofilms were back to nearly the same susceptibility levels as original mature biofilm. Walcott et al (2010) conclude that the findings of this study demonstrate the principles of BBWC including: regular effective debridement, followed by topical antimicrobials. A retrospective observational study carried out by Nakagami et al (2020), uses wound blotting technology to identify biofilms within non-healing pressure ulcers (PU). When the wounds in this study were sharp debrided to eliminate biofilm, wound healing was significantly improved compared with those where a biofilm remained. There were nine patients included in the study and the percent area decrease was significantly higher in the debrided group (14.4%; range: 4.6 to 20.1%) than in the control group (–14.5%; range: –25.3% to –9.6%; p=0.050). There were also lower levels of biofilm detection after the debridement, which correlated with the area decrease (coefficient= –22.84; p=0.040). This study supports the conclusions of Wolcott et al (2010) and again demonstrates the importance of optimal debridement when treating wounds biofilms.

Evidence behind the use of monofilament fibre debriding technology

While several studies and consensus documents recommend sharp debridement for the removal of biofilm (Walcott et al, 2010; Bianchi et al, 2016; Nakagami et al, 2020), this form of debridement is dependent on the availability of staff qualified to perform the procedure. In general, in the community setting, there are limited staff who are qualified to carry out sharp debridement, hence this is often not a practical or feasible treatment option. Therefore, effective alternative debridement options need to be considered. A number of studies aimed to examine the clinical efficacy of monofilament fibre debriding technology (MFDT) as an effective alternative to sharp debridement (Bahr et al 2010; Roes et al, 2019a; 2019b), an example of which can be seen in *Figure 1*). These studies were of similar design, prospective, non-controlled, observational studies designed to assess wound outcomes following the



Initial injury 9 November 2020. On 20 November debridement was started twice a week, with an MDFT pad

14 January 2021 (after 8 weeks of treatment)

11 March 2021 (after 16 weeks of treatment)

Figure 1. Illustrating the use of monofilament fibre debriding technology (MDFT). A patient with a non-healing wound (incurred 9 March 2020), began with 2 x weekly debridement with MDFT on 20 November

use of MFDT for debridement, including clinician and patient satisfaction. In the Bahr et al (2010) study clinicians (n=57) used a debridement pad (Debrisoft©, L&R) during their wound care practice over a 12-day period. Clinician assessment indicated that the product was found to be effective at removing debris, slough and dried exudate efficiently without damaging the periwound skin. In addition, patients reported minimal pain or discomfort. These statements were supported by digital photos taken throughout the study and rated by a blinded, independent clinician. The mean duration of MFDT debridement was also compared with other debridement methods (surgical, mechanical with gauze and autolytic debridement), all of which were found to take significantly longer ($p<0.05$). These findings are largely replicated in two studies by Roes, Calladine and Morris (2019a; 2019b) with high ratings of clinician satisfaction and reports of reduced wound size. The second study by Roes, Calladine and Morris (2019b) had a longer 2-week evaluation period in which MFDT was used as part of a biofilm pathway (debridement was followed by use of an antimicrobial dressing alongside other care such as secondary dressings and compression according to local guidelines) and significant wound improvement was reported. These three studies concluded that MFDT has potential to replace other methods of debridement based on its efficacy, short procedure, ease of use and patient comfort and suggest the use of MFDT as part of a BBWC pathway. It is important to note that these studies were funded by the product manufacturer and while this is declared the potential for bias must be considered.

MFDT compared with gauze

Anecdotally, in many areas of current practice in the community setting, wounds tend to be cleansed and mechanically debrided by use of gauze alone, with the use of MFDT often limited and not always available on a formulary. Wilkinson et al (2015) aimed to evaluate and directly compare the efficacy of MFDT versus the use of gauze within a *ex vivo* porcine study. This study directly compared three alternatives for mechanical debridement, 2 monofilament pads — Debrisoft, Debrimitt and gauze. Like Wolcott (2010), this study used *Pseudomonas aeruginosa* and *Staphylococcus aureus* to culture 48-hour old established biofilm. Debriding devices were all attached to a mechanical cleaning device, and it was shown that both polymer devices significantly reduced biofilm (Debrisoft $p=0.01$; Debrimitt $p=0.003$) and outperformed gauze ($p=0.067$) with up to 100-fold greater reduction in bacterial counts. A further *in vitro* study by Weigland et al (2017), also compared the efficacy of MFDT to that of gauze. Debridement methods were trialled on three samples with differing levels of protein, which was applied *in vitro* to resemble different levels of wound slough. The findings demonstrated that the cleansing ability

of gauze and MFDT were comparable at a lower protein rating 0.5% bovine serum albumin (BSA), MFDT performed significantly better (p=<0.05) at a moderate protein concentration (1% BSA) and, when wiping duration was increased, MFDT also performed better in a higher protein concentration (1.5% BSA). These studies establish that MFDT is more effective than commonly used gauze swabs and therefore could be recommended as part of a BBWC pathway in the community setting. Both Weigland et al (2017) and Wilkinson et al (2015) declare funding from the product manufacturer(s) so as previously mentioned the potential for bias must be considered.

Wound cleansing

Depending on the wound type, wound cleansing in the community setting, is usually carried out with tap water, sterile water or saline and, less frequently, with solutions containing surfactants. Surfactants lower the surface tension between a liquid and a solid, such as debris and biofilm, helping to disperse the latter, which can then be removed more easily with a cleansing pad or cloth. Multiple consensus documents and researchers recommend the use of antiseptic surfactant solutions to cleanse the wound and periwound area, with a soak time of 10–15 minutes, as saline or water have not been evidenced to remove biofilms (Bianchi et al, 2016; Malone and Swanson, 2017; Murphy et al, 2020; IWII, 2022). While the ideal wound cleansing solution, in the presence of biofilm, has not been established conclusively, a surfactant with antiseptic agent included, may be beneficial, as part of a BBWC pathway, to both aid effective debridement and to increase penetration of antimicrobial agent to the wound bed. It is vital that thorough wound cleansing is carried out at each dressing change, which would include both the periwound area and the wound bed.

Antimicrobial dressings

Following cleansing and debridement, BBWC pathway recommendations are for the use of antimicrobials, specifically antiseptics, to supress the reformation of biofilm (WUWHS, 2016; Shultz et al, 2017; Murphy et al, 2020). As biofilms are intrinsically resistant to antimicrobial treatment, the application of any antimicrobial dressing must be carried out following thorough cleansing and debridement, to prevent the spread or reformation of a biofilm rather than to treat an established biofilm (WUWHS, 2016; Shultz, 2017). Available antimicrobial dressings include honey, iodine and silver which are all widely available in various forms and commonly used in the community setting. Antimicrobial dressing choice would depend on a holistic assessment of the patient and their wound. Due to growing global concern regarding antibiotic resistance, the use of topical antibiotics within a BBWC pathway is not recommended and topical or systemic antibiotics should only be considered when clinical infection is suspected or confirmed, in line with antibiotic stewardship guidelines (Metcalf and Bower, 2013; Shultz et al, 2017; IWII, 2022). For similar reasons, a 'step-up, step-down' approach should also be used with any antimicrobial dressings, with regular re-assessment of the effectiveness of treatment, ideally every two weeks, to both ensure optimal treatment is maintained and to discontinue the use of antimicrobial dressings once they are no longer required (Shultz et al, 2017; Murphy et al, 2020).

Antibiofilm agents

A new area of research gaining interest and highlighted as potentially useful in the treatment of a biofilm, is that of biofilm disrupting agents (Miller et al, 2014; WUWHS, 2016; Weigelt et al, 2020; IWII, 2022) that target the biofilm EPS matrix. Studies by Wolcott (2015) and Kim et al (2018), in particular, have looked at an antimicrobial wound gel (BlastX), composed of benzalkonium chloride 0.13%, polyethylene glycol, sodium citrate, citric acid and water, which inhibits biofilm development and disrupts biofilm defences by disrupting quorum sensing, supressing and degrading EPS and blocking attachments (Wolcott, 2015; Weigelt et al, 2020). Wolcott (2015) conducted the first clinical study using this biofilm-disrupting gel (BlastX, Next Science), in which participants were randomised into three groups: standard care (SC), who received weekly sharp debridement plus topical antibiotics (n=15); wound gel only, who received the wound gel three times weekly (n=15); SC plus wound gel, who received both strategies (n=15). The study, carried out over four weeks, showed that wound volume reduction and wound healing (using the surrogate end point of 50% reduction at four weeks) were both significantly improved when antibiofilm wound gel was used, to degrade the biofilm matrix, with the

highest levels of success when used in conjunction with SC. It is important to note that while topical antibiotics were used as part of this study, this, as discussed, is not recommended in practice. As part of a BBWC pathway, topical antibiotics would need to be used with caution and always under prescription with clear start and stop dates. Kim et al (2018), in a study sponsored by the manufacturer, carried out a follow up 12-week trial, in which chronic, recalcitrant wounds (n=43) were sharp debrided and then treated with biofilm disrupting wound gel (BlastX) experimental group or a broad-spectrum topical antibiotic, control group. This resulted in a significant wound size reduction and wound closure in the experimental group ($p \leq 0.01$), closure, in this place, being defined as 90% wound reduction, with wound area, volume and depth measurements taken using the Silhouette Star camera (ARANZ Medical, Christchurch, New Zealand).

RECOMMENDATIONS FOR PRACTICE

The evidence is clearly pointing to a BBWC pathway being introduced into community practice (*Figure 2*). A BBWC pathway should be considered for all patients with non-healing wounds (following a holistic assessment that addresses other factors that may delay wound healing). This BBWC pathway would include the use of MFDT for debridement, for use 2–3 times weekly, particularly in wounds with high levels of slough or necrosis, due to its efficacy when compared with gauze, and sharp debridement not always being easily accessible within the community setting. The inclusion of MFDT in dressing formularies or similarly effective debridement agent is important,

Figure 1. Biofilm treatment pathway for the community setting (adapted from WUWHS, 2016; Shultz et al, 2017; Murphy et al, 2020)

with the ultimate aim of increasing the occurrence of regular effective debridement. Another dressing formulary recommendation would be the inclusion of an antiseptic surfactant solution for wound cleansing. This would be followed by use of a topical antimicrobial dressing (excluding topical antibiotics) and any necessary adjunct therapies, such as compression, as per local guidelines. It is vital that the effectiveness of the treatment is reviewed regularly, ideally every two weeks, to ensure optimal treatment is maintained as well as stepping down antimicrobial treatment when appropriate, e.g. wound starts to heal, parameters for this should be documented in the patient's notes. Educational sessions for staff members would be a central element in the introduction of a BBWC pathway, ensuring all staff understand the rationale and importance of following this treatment pathway and the potential positive impact on wound healing outcomes. Documented communication of the treatment each patient is receiving and the date when a review of treatment is due would also be vital due to an ever-changing flow of staff who may not know the patients they are seeing. A future area of interest and possible use in practice would be the introduction of a biofilm disrupting wound gel. More research is needed in this area, though the studies discussed in this article would indicate that a biofilm disrupting wound gel could be a useful addition to the future of BBWC pathways. WUK

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