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Comparison of five dermal substitutes in full-thickness skin wound healing in a porcine model

Cécile Philandrianos [a,*], Lucile Andrac-Meyer [b], Serge Mordon [c], Jean-Marc Feuerstein [d], Florence Sabatier [e], Julie Veran [f], Guy Magalon [f], Dominique Casanova [f]

[a] Department of Plastic Surgery, Hôpital Nord, Chemin des Bourrely, 13915 Marseille, France
[b] Department of Pathological Anatomy, Hôpital Nord, Chemin des Bourrely, 13915 Marseille, France
[c] INSERM, U 703, Univ Lille Nord de France, Lille University Hospital, Loos, France
[d] Laboratory of Animal Experimentation, Faculty of Medicine La Timone, Marseille, France
[e] Laboratoire de culture et thérapie cellulaire CIC BT 510, Centre Hospitalier Universitaire la Conception, Marseille, France
[f] Department of Plastic Surgery, Hôpital de la Conception, 13005 Marseille, France

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ABSTRACT

The wound healing attributes of five acellular dermal skin substitutes were compared, in a two-step procedure, in a porcine model. Ten pigs were included in this experimental and randomized study. During the first step, dermal substitutes (Integra®, ProDerm®, Renoskin®, Matriderm® 2 mm and Hyalomatrix® PA) were implanted into full-thickness skin wounds and the epidermis was reconstructed during a second step procedure at day 21 using autologous split-thickness skin graft or cultured epithelial autograft. Seven pigs were followed-up for 2 months and 3 pigs for 6 months. Dermal substitute incorporation, epidermal graft takes, wound contraction and Vancouver scale were assessed, and histological study of the wounds was performed.

Results showed significant differences between groups in dermis incorporation and in early wound contraction, but there was no difference in wound contraction and in Vancouver scale after 2 and 6 months of healing.

We conclude there was no long-term difference of scar qualities in our study between the different artificial dermis. More, there was no difference between artificial dermis and the control group. This study makes us ask questions about the benefit of artificial dermis used in a two-step procedure.

1. Introduction

In full-thickness skin wound healing, dermal reconstruction is fundamental to optimize the functional and esthetic outcome. Usually, full-thickness skin graft or flaps are used to reconstruct the dermis. When the full-thickness skin wound is large, like in burn patients, the dermis cannot be reconstructed by classical plastic surgery techniques but it can be reconstructed by allograft skin [1]. An alternative is the use of artificial dermal substitutes [2].

Dermal substitutes are scaffolds composed of extracellular matrix components: collagen and glycosaminoglycan or hyaluronic acid. Their composition and their thickness

* *Corresponding author at*: Service de Chirurgie Plastique et maxillo-facicale, Department of Plastic Surgery, Hôpital Nord, Chemin des Bourrely, 13915 Marseille Cedex 20, France. Tel.: +33 491 968 690; fax: +33 491 964 350.
E-mail addresses: Cecile.philandrianos@ap-hm.fr, cecphil@gmail.com (C. Philandrianos).
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(1–2 mm) are variable. Some of them can be coupled to a silicone film.

Usually, the dermal substitutes are covered by an autologous split-thickness skin graft in a two-step procedure performed 21 days after dermal substitute grafting [3]. This delay is necessary to obtain neovascularization and incorporation of the matrix. When the scaffold is vascularized, it is able to provide blood supply to the skin graft.

Some dermal substitutes like Matriderm® 1 mm can be used in a one-step procedure: the dermal substitute is immediately covered by an autologous skin graft [4]. In this case, autograft survival is not altered by simultaneous application of the dermal matrix because the dermal substitute is thin (1 mm) and the wound can feed the graft through the matrix. The main interest lies in the one step procedure; its disadvantage is the thinness of the reconstructed skin.

Dermal substitutes have been developed for 30 years [5]. Integra® dermal regeneration template (Integra LifeSciences Services, USA) has been for many years the only dermal substitute commercialized, but recently several new artificial dermis have been developed [6]. Unfortunately, no study exists that compares the different substitutes in skin wound healing, except in a mouse model [7] and in a rat model [8]. However, data provided into the literature [9–11] are not sufficient to compare these different substitutes.

The reference model in skin wound healing studies is the pig model [12–14]. This model is used by most teams studying artificial dermis [15–17]. The interest of this model is that it can be used to treat large wounds, with size similar to human beings.

That is why we conducted an experimental randomized study in a porcine model, which aimed to compare the wound healing attributes of five artificial acellular dermal skin substitutes (Integra®, ProDerm®, Renoskin®, Matriderm® 2 mm® and Hyalomatrix® PA), in a two-step procedure. Different dermal substitutes were implanted into full-thickness skin wounds during the first step, and after 21 days, the epidermis were reconstructed using autologous split-thickness skin graft or cultured keratinocytes.

2. Materials and methods

2.1. Animal models

Ten female Large-White (Yorkshire) pigs, weighing approximately 20–25 kg each, were studied and kept under standard conditions in the animal care unit in Marseille ‘‘Timone Medical University’’. The protocol was approved by the experimental ethic committee.

2.2. Anesthesia

The pigs were sedated by intramuscular injection with ketamine 10 mg/kg, stressnil and 1 μg/kg atropine. Complete anesthesia was induced with an intravenous perfusion of propofol. The animals were incubated and artificial respiration was applied. During the surgery, analgesia was provided by intramuscular injections of morphine.

2.3. Artificial dermis preparation

Five acellular artificial dermis were chosen to be compared; all of them had to be used in a two-step procedure:

- Integra® dermal regeneration template (Integra LifeSciences Services, USA) is a 2.1 mm thick bi-laminar skin substitute composed of a layer of bovine tendon collagen type I matrix and shark chondroïtine-6-sulfate and a silicone layer that acts as a temporary pseudo-epidermis [3],
- Renoskin® (Symatèse, France) is a 2 mm thick bi-laminar skin substitute composed of a bovine collagen matrix type 1 and a strengthened silicone film [16,18],
- Matriderm® 2 mm (Skin & Health Care, Germany) is a 2 mm thick lyophilized single-laminar matrix of bovine collagen type 1, 3, 5 with elastin [4],
- ProDerm® (Laboratoire Genévrier, France) is a 2 mm thick equine collagen matrix type 1, chitosan and chondroitin sulfates [17,19],
- Hyalomatrix® (Fidia Advanced Biopolymers, Italy) is a 2 mm thick esterified hyaluronic acid fiber matrix beneath a silicone membrane [20,21].

Prior to use, Renoskin®, ProDerm®, Matriderm® were rehydrated in physiological saline solution for a few minutes and Integra® was rinsed with physiological serum for a few minutes.

2.4. Wound healing and dermal reconstruction

On day 0, each pig was anesthetized and placed in a ventral recumbent position. The surgical site was cleaned with betadine® and the animals were administered a prophylactic antibiotic (amoxicillin). Twelve 16 cm^2 full-thickness excision wounds were performed on the dorsum of each animal. The borders of each 4 cm × 4 cm paraspinal defect were marked with a tattooing device.

Each wound was either immediately implanted with one of the five acellular dermal substitutes (previously cut to the size of the wounds with scissors) or assigned to the control group with no dermal substitute using a randomization scheme to avoid site bias. Matrices were held in place with skin staples. Wounds were primarily dressed with Adaptic®, and were covered with compresses. The dorsum of the animal was secured with elastic tape.

Every week, the animals were anesthetized to change the dressing and to perform a gross wound observation, including digital photographies. The silicone films were removed when complete detachment of the pseudo-epidermis was noted.

Artificial dermis integration gross observations were recorded at day 14.

2.5. Epidermal reconstruction

21 days after surgery, each pig was anesthetized again, placed in a ventral recumbent position and the surgical site was cleaned with betadine®. All wounds (including the control wounds) were prepared for application of epidermal autograft by excising, with a surgical blade, any epithelia from the wound periphery. Hemostasis was obtained through cauterization.