

# Dehydrated Human Amnion/Chorion Membrane Tissue Graft for the Treatment of Intractable Ulceration: A Series of Extraordinary Outliers

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## Abstract

Chronic non-healing wounds are a significant challenge for patients and healthcare providers. Annually, treatment of these wounds costs billions of dollars worldwide (1,2). Treatment options include both preventative methods and intensive treatment strategies. Human amniotic membrane has been used in the treatment of wounds for over a century (3). Recently there have been improvements to the processing of dehydrated human amnion/chorion membrane (dHACM) which have resulted in a graft that is capable of being stored at ambient temperature for up to five years (4). In this six patient case study, we examined the versatility of this type of graft in healing intractable lower extremity wounds of a vascular etiology. We chose patients with wounds remaining unhealed for a minimum of one year and had failed a variety of other treatments. The group contained six wounds (five venous leg ulcers and one diabetic foot ulcer) which had been present for between one and eleven years (average of 4.78 years). Five of the wounds had been unsuccessfully treated five times with a bioengineered skin substitute, and in addition two wounds had been treated with radiation due to squamous cell carcinoma. Treatment consisted of waiting one month after final application of the bioengineered skin substitute, tissue biopsy for culture, debridement, and conventional wound care. We applied dHACM after sharp debridement as needed, followed by standard topical dressings. Patients were assessed weekly for wound closure. Of the four wounds that were healed by the time of publication, there were an average of 3.5 applications of dHACM in an average of 7.5 weeks and an average initial wound size of 16 cm<sup>2</sup>. The effectiveness of the dHACM graft for non-healing lower extremity ulcerations along with its long shelf life and ease of use make it an effective treatment choice for chronic wounds.

## Background

Treatment costs related to the management of chronic non-healing wounds reach billions of dollars annually. (1,2) Management strategies that can promote rapid and complete healing of chronic wounds can significantly reduce risk of additional complications and reduce overall health care costs.

Human amniotic membrane has been used in the treatment of wounds for over a century. (3) Recently there have been improvements to the processing of human amniotic membrane resulting in a commercially available dehydrated human amnion/chorion membrane (dHACM\*) allograft that comes in various sizes and is capable of being stored at ambient temperature for up to five years (4). PURION® processed dHACM has been shown to contain many growth factors that help in wound healing, including PDGF-AA, PDGF-BB, bFGF, TGF-β1, EGF, VEGF, and PIGF. (5) In addition to growth factors, cytokines including anti-inflammatory interleukins (IL-1ra, IL-4, IL-10) and the TIMPs (TIMP-1, TIMP-2, TIMP-4) which help regulate the matrix metalloproteinase (MMP) activity are also present in dHACM. (5) Results from *in vitro* and *in vivo* experiments clearly established that dHACM contains one or more soluble factors capable of stimulating local mesenchymal stem cell migration and recruitment. PURION® processed dHACM has been shown to retain biological activities related to wound healing, including the potential to positively affect four distinct and pivotal physiological processes intimately involved in wound healing: cell proliferation, inflammation, metalloproteinase activity, and recruitment of local progenitor cells. (5) A previous randomized study has shown the efficacy of using dHACM for the treatment of diabetic foot ulcers with healing rates of 77% and 92% within 4 and 6 weeks of treatment initiation respectively. (6)

## Study Design and Purpose

In this six patient case study, we examined the versatility of dHACM allograft in healing intractable lower extremity wounds of a vascular etiology.

## Methods

### Included

- ❖ Patients with wounds remaining unhealed for a minimum of one year and had failed a variety of other treatments.
- ❖ The group contained six wounds (five venous leg ulcers and one diabetic foot ulcer) which had been present for between one and eleven years (average of 4.78 years).

### Treatment

- ❖ Five of the wounds had been unsuccessfully treated five times with a bioengineered skin substitute (BSS), and in addition two wounds had been treated with radiation due to squamous cell carcinoma.
- ❖ Treatment consisted of waiting one month after final application of the bioengineered skin substitute, tissue biopsy for culture, debridement, and conventional wound care.
- ❖ We applied dHACM after sharp debridement as needed, followed by standard topical dressings.
- ❖ Patients were assessed weekly for wound closure.

### Investigators

- ❖ SDJ was the attending physician, JT was chief resident, and DM was 2<sup>nd</sup> year resident.

## Results

- ❖ 5 of the 6 intractable wounds in this case series healed with dHACM.
- ❖ These 5 wounds were present for an average of 5.6 years and healed in an average of 13.5 weeks with 5.5 dHACM allografts.

### Case 1: Radiation wound. Chronic for 11 yrs



### Case 3: Radiation wound. Chronic for 2 yrs



## Results

Table 1. Patient characteristics.

Case	Gender/Age	Wound Location	Chronicity	Wound Size at 1 <sup>st</sup> dHACM	Time to Healed	# dHACM	Comments
1	M / 72	L Leg r/t squamous cell CA Radiation	11 yrs	7.0 x 7.5 x 0.2 cm	19 weeks	8	Wound did not close with BSS x 5. Obesity, PAD, Lymphoma
2	M / 86	L Heel	3 yrs	0.5 x 0.1 x 0.1 cm	2 weeks	1	Wound did not close with BSS x 5. Diabetic, PAD, Neuropathy
3	M / 85	R Leg r/t squamous cell CA Radiation	2 yrs	3.8 x 2.0 x 0.4 cm	24 weeks	8	Wound did not close with BSS x 5. PAD, HTN
4	F / 75	L Leg r/t squamous cell CA	5 – 7 yrs	3.5 x 1.7 x 0.2 cm	4 weeks	2	Wound did not close with BSS x 5. Obesity, HTN.
5	M / 67	L Ankle r/t trauma from accident	5 – 7 yrs	3.0 x 1.9 x 0.1 cm	5 weeks	3	Wound did not close with BSS x 5. Neuropathy, Post-Phlebitis Syndrome.
6	F / 70	L Ankle r/t PAD	1 yr	3.5 x 2.0 cm	Ongoing		Multiple medical complications. End stage MS. Never received BSS. Refuses BKA.

CA = cancer; PAD= peripheral artery disease; MS = multiple sclerosis; BKA = below knee amputation; BSS=bioengineered skin substitute.

## Conclusions

- ❖ The effectiveness of the dHACM graft for non-healing lower extremity ulcerations along with its long shelf life and ease of use make it an effective treatment choice for chronic wounds.
- ❖ In this case series we examined the use of dHACM for the treatment of difficult intractable wounds. We found that difficult wounds failing to heal after treatment with a bioengineered skin substitute, even those wounds secondary to radiation, responded and healed with dHACM treatment.

## References

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\*dHACM = EpiFix®, MiMedx Group, Inc., Marietta, GA

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