

LETTER TO THE EDITOR OPEN ACCESS

Response to Commentary on “Cryopreserved Total Skin Allografts From Living Donors for Complex Wound Management: A New Paradigm in Regenerative Wound Care”

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Dear Editor,

We thank Ma et al. for their thoughtful comments regarding our article on cryopreserved total skin allografts (CTSA) derived from living donors [1]. Their observations provide an important opportunity to clarify several conceptual and methodological aspects of our work.

First, we agree that the term viable allografts used in our original publication may not accurately reflect the biological status of CTSA. Because our protocol incorporates terminal gamma irradiation (25–28 kGy), and formal viability assays were not performed, we believe that these grafts should currently be interpreted as structurally preserved but biologically active, rather than viable from a cellular perspective [2, 3].

Importantly, despite the expected reduction in cellular viability associated with terminal irradiation, both our clinical observations and previous experimental evidence suggest preservation of dermal architecture and the capacity of the extracellular matrix to interact with the host immune response [2, 3]. In this context, we believe that the principal therapeutic value of CTSA may reside more in the preservation of the dermal extracellular matrix as a biologically active scaffold capable of interacting with the host immune response and less in donor cell survival.

We also appreciate the comments on microbiological governance and cold-chain resilience. Our protocol incorporates sequential microbiological surveillance at four defined processing stages (M0: post-procurement, M1: post-initial processing, M2: during processing, and M3: pre-packaging), combined with strict cold-chain management and terminal gamma irradiation prior to clinical release. The microbiological profile observed in our study was dominated by low-virulence commensal organisms associated with resident skin flora from living donors undergoing elective surgery rather than nosocomial pathogens. The microbiological discard rate was 4%, which is below the lower range reported in the literature for cadaveric skin banking. Furthermore, the only major storage-related incident corresponded to an isolated power failure and backup system malfunction rather than a transport failure, despite the long geographic distances involved in Chile. Corrective measures implemented after this event included redundant real-time temperature monitoring, independent validation sensors, alarm escalation protocols, and thermal mapping of ultra-low freezers [4, 5].

Regarding the regenerative interpretation of CTSA, we fully acknowledge that the mechanisms underlying the observed “neodermis-like” tissue remain incompletely understood. Nevertheless, the consistent clinical pattern observed in our

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series, characterized by initial graft adherence, subsequent superficial eschar formation, and persistence of vascularized tissue beneath the epidermal component, suggests that CTSA may participate in a host remodelling process more complex than simple temporary coverage. In this regard, historical observations from Medawar, Yang, Cuono, Langdon, and others have suggested that the dermal component of skin allografts may exhibit biological behaviour distinct from the epidermal component [6–9]. Our findings are consistent with this concept and support the hypothesis that preserved dermal architecture may contribute to tissue organization and regeneration. However, we fully agree that additional mechanistic studies, including cellular tracing, immunohistochemical characterization, and evaluation of host–donor interactions, are necessary before definitive conclusions can be established.

Finally, we agree that future studies should incorporate standardized clinical endpoints, including time to definitive closure, infection recurrence, need for reoperation, quantitative graft take, scar quality, functional outcomes, and patient-centered outcomes. Comparative analyses with other biological and dermal substitutes will also be important to define the specific clinical value of CTSA within reconstructive algorithms. An expanded clinical series with longitudinal follow-up is currently being prepared. In addition, a systematic evaluation of sensitization phenomena associated with repeated applications will be incorporated into future prospective protocols [10].

We sincerely appreciate the authors' interest in our work and believe that the questions raised by Ma et al. will help guide the next phase of investigations in this emerging field [11].

Conflicts of Interest

Marcelo Fonseca is the inventor of a patent related to the Cryopreserved Total Skin Allografts (CTSA) described in this article. This patent has been granted in Japan, Canada, and Australia and is currently under examination in other jurisdictions. The author declares that he has not received royalties, financial compensation, or any other economic benefits from this patent.

Data Availability Statement

Data sharing not applicable to this article as no datasets were generated or analysed during the current study.

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