Endovascular Management of Severe Peripheral Artery Disease By Smart Stem Cell Delivery Technology

Prof Sherif Sultan¹,²
MD FRCS FACS PhD
Professor of Vascular & Endovascular Surgery
Chairman of Western Vascular Institute
Vascular & Endovascular Clinical Lead Saolta Trust

1. Western Vascular Institute, UHG⁹⁸¹⁴,G, Ireland
2. Galway Clinic⁸⁸⁺, Galway, Ireland
Disclosure

- Founder of Tulip Endovascular Innovation, Ireland
- Founder of Embricon Endovascular, Ireland
- Founder of Green Medical, Michigan, USA
- Research Education Grants:
  - Cordis, Medtronic, Endologix, Gore, Vascular Solutions
  - BMS, MSD, AstraZeneca, Cardiatis, Abbot, AOTI
  - Sanofi-Aventis, Pfizer, Ulbrich, Bolton Medical
  - SFI, EI, NSAI, HRB
Cell-based Therapies were Developed in The Hope Of Translating Laboratory-based Technology Into Clinical Successes, However Clinical Results Have Been Disappointing

All Major Trials Failed To Meet Their High Expectations, While Second-generation Trials Have Been Associated With Adverse Effects
The TRAFFIC & The RAVE Trails, Both Utilized Intramuscular Injection

The START Trail Used Subcutaneous Injection

None of These Trials Showed Any Improvement In Walking Capacity & All Three Failed To Meet Their High Expectations

These Therapies Have Been Associated With Serious Adverse Side Effects

The Main Culprit is The Method of Stem Cell Delivery
90% of PAD Never Progress to CLI, Which Makes it Apparent That There is Something Indolent About CLI That Makes Them Susceptible to Limb Loss & A Priority For Therapeutic Target

Equally There May Be A Protective Mechanism in Claudicants, Which Defends Them From The Risk of Limb Loss

CLI Cure Remains An Unmet Clinical Need
Choice of Bypass or Endovascular in CLI Must Address The Ischemic Capillary Bed Status. Revascularization, Regardless of the Method, Does Not Guarantee Limb Salvage Within One Year

Different Strategic Modalities of Recruiting & Enhancing of Capillary Bed Prior To Any Intervention is Mandatory
After 850 Million Dollars; Placebo Effect is As Good As Stem Cell Therapy
Bioengineered Microspheres
Prolong, Recruit & Improve Regenerative Activities of Bioactive Factors & Resident Stem Cells
This System is Designed for Localized Cell Delivery & to Serve As Scaffold for Increasing Cell Retention & Infiltration
Lidocaine, Heparin & Flow delivery was found to be Toxic & Results in 75% Fewer Live Stem Cells
PVD Stem Cell Trials Are Lacking A Global Solution For A Standardized Delivery System For Any Type of Stem Cell Therapy

The Failure of Intra-muscular & Intra-arterial Injection Had Raised Concern For The Biotech Industry About Their Ability To Carry On Clinical Trials & Sustain Their Current Multi-billion Dollar Market

Intra-venous Heparin & Local Anesthetic Like Xylocaine Have Proven Fatal To Stem Cells & Both Are Mandatory To The Current Delivery Method

A Smart Stem Cell Delivery System is Required to Overcome Limitations In Stem Cell delivery
Unmet Healthcare Need

- Current Methods Of Delivery Of Stem Cell Therapies Lack Global Standards, The Ability To Ensure Delivery To Target Areas & A Smart Solution To Enhance & Augment The Survival of The Delivered Stem Cell

- Our Smart Management System Is The Only Treatment Available To Deliver The Stem Cells From Any Manufacturer To The Target Area With Minimal Disruption To The Physiological Media That Harnesses The Ability Of Stem Cell To Survive
Smart Stem Cell Delivery System Is Directed Towards Optimizing Delivery of Therapeutic Agents Into The Venous System With An Endpoint of Relieving Arterial Blockages By Promoting Angiogenesis

These Agents Are Perfused Into The Venous System To Promote Angiogenesis Within The Arteries Via Capillary Networks

The Novelty of This Device is Arterio-venous Manipulation
The System Is Adapted To Deliver The Therapeutic Agent By Infusion Under A Pressure Of Up to 90 mmHg, Adjusted According To The Wire Sensor To Over Come The Peripheral Resistance & Does Not Crush Stem Cells

The Automated Device Has A Processor, Valves Incubator Like Environment And Timers For Controlling The Required Delivery Parameters

Stem Cell Released Under Mechanical Or Electronic Control, Depending On The Flow Rate Calculated In Response To The Pressure Required To Push The Stem Cell From The Veins To The Arterioles
The System is Adapted To Deliver Different Therapeutic Agents in Successive Stages Each With a Corresponding Set of Delivery Parameters
Stage One: Include An Elixir Stem Cell Solution To Open Collapsed Venules & Prepares The Meta Capillaries For Receiving Platelet Rich Plasma, Which Will Act As Nourishment For The Stem Cells

Stage Two: A Platelet-rich Plasma To Prepare The Vascular Bed For Delivery Of Stem Cells & Growth Factors In Stage Three

Stage Four: Is Delivery of Fibrinogen Scaffold That Allows The Stem Cell To Adhere Directly To The Desired Tissue

Stage Five: Is The Stem Cell Elixir That Keeps The Precious Stem Cells in The Target Area
Our Novel Smart System Offers A Disruptive Technology For Site Specific Delivery of Therapeutic Agents Into The Arterio-venous System

This Delivery Device does not Disturb Any Occlusion or Atheromatous Plaque Or Thrombus, Evading The Risk of Embolic Material Being Released Distally

Delivery Through Anti-grade or Retro-grade Approach Through the Tibial Vena committantea, With An Endpoint of Manipulating the Arterio-venous Junction By Promoting Angiogenesis/ Vasculargenesis
Critical appraisal of stem cell therapy in peripheral arterial disease: Do current scientific breakthroughs offer true promise or false hope?

Sherif Sultan1,2, Niamh Hynes1

1Department of Vascular & Endovascular Surgery, Western Vascular Institute, University Hospital Galway, Galway, Ireland
2Department of Vascular and Endovascular Surgery, Galway Clinic, Doughiska, Galway, Ireland

Received 31 December 2013; revised 3 February 2014; accepted 10 February 2014

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ABSTRACT

Over the last forty years in the field of peripheral arterial disease, there has been a plethora of research into cell-based therapies for tissue repair, regeneration and angiogenesis, progressing from protein-based therapies to gene therapies to stem cell research. Initial pre-clinical research successes have given birth to a whole industry, aimed at translating these laboratory hopes into clinical studies. However, many of these expected clinical results have failed to materialize, in part due to the lack of attention to the ischaemic, non-invasive nature of the disease. In some instances, an otherwise promising clinical study has failed to confirm the previous preclinical results, leading to interruptions in patient recruitment. In this review, we examine the clinical evidence for angiogenic therapies, focusing specifically on stem cell trials. In an attempt to answer the question “Is stem cell therapy a failed experiment or will there be light at the end of the tunnel?”

KEYWORDS

Peripheral Arterial Disease; Stem Cell Therapy; Therapeutic Angiogenesis

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5. CELL THERAPY DELIVERY; THE FUTURE

Stem cell research is in its infancy and there are many questions to be answered before we can hope that this treatment option will provide acceptable clinical outcomes and sustainable results.
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