UNRAVELLING PATIENT PREDICTORS OF MESENCHYMAL STEM CELLS EXPANSION IN AN ORTHOPAEDIC SETTING

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Introduction

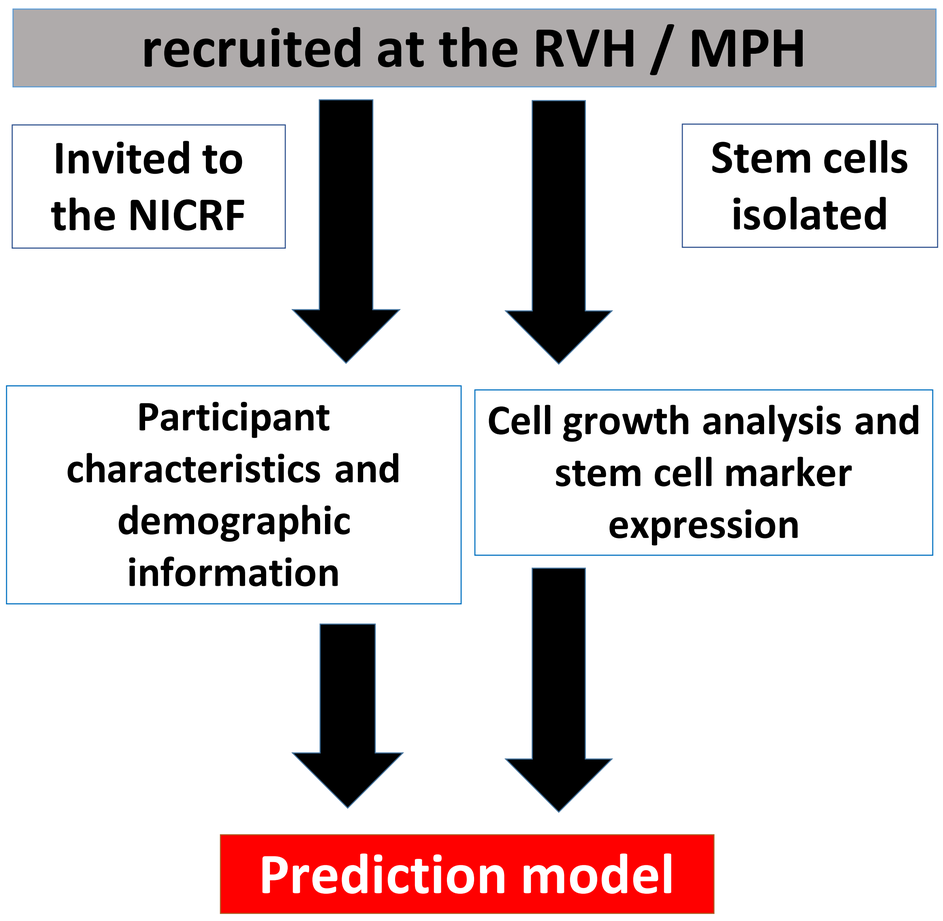
Stem cells have the capacity to self-renew and generate differentiated cells. Mesenchymal stem cells (MSCs) are pluripotent cells that can differentiate into the cell lineages derived from the mesoderm: osteoblasts, chondroblasts and adipoblasts[1]. MSCs are present in almost every tissue but are most prevalent in adipose tissue, marrow, dental pulp and neonatal tissue.

Endocrine pathways like the fat/bone and GH/IGF-1 axes alongside physical strain influence the recruitment of MSCs to each of the cell lines, studies have found a link between BMI and MSCs osteogenesis in men[3].

MSCs have been used clinically for therapeutic affect to treat a wide range of conditions including: cardiovascular disease, bone defects, Parkinson's disease and acute burns[4,5]. Autologous treatments which utilise a patient's own cells expanded in-vitro avoid the risk of Graft versus host disease but are limited by the cells' potency and ability to expand.

Project Aim

The aim of this project is to explore the characteristics that affect MSC growth and build a prediction model that can estimate growth capability based on less invasive measures than requiring a marrow aspirate.



Methods

Bone marrow samples were collected from participants recruited from Royal Victoria Hospital and Musgrave Park Hospital undergoing interpedical screw surgery. Cells are isolated using density centrifugation method. Once in culture, measures of cell performance and MSC characterisation were conducted, including colony forming unit assays, alkaline phosphatase expression and activity, MSC specific antibody marker expression and growth curve analysis.

Participants were also asked to complete a diet and lifestyle questionnaire, a body stat assessment for body composition (fat % etc.), urine, saliva and blood sample collection to test for bone and fat turnover markers. Once all samples are collected, the blood serum, urine and saliva will be tested for levels of ghrelin, obestatin, leptin and adiponectin, hormones associated with the fat/bone axis.

Combining the stem cell sample outcome measures with the participant characteristics a prediction model will be developed to predict MSCs ability to expand for autologous cell therapy.

Results

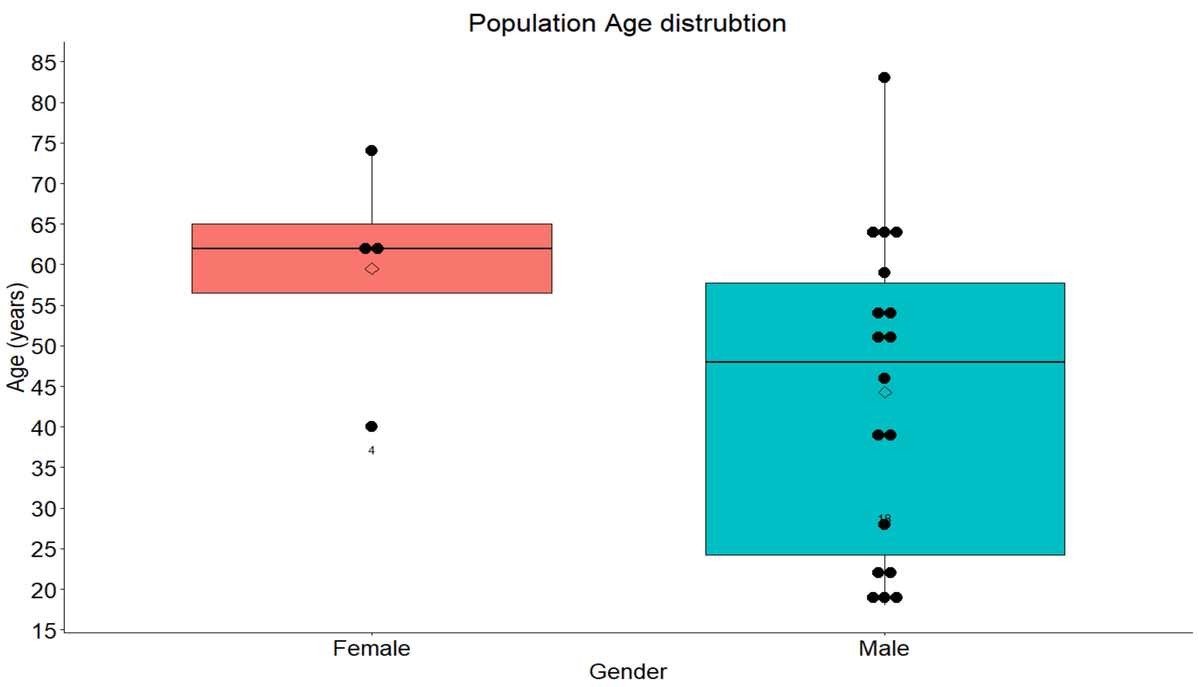


Fig. 1 Participant population age distribution.

4 Female recruits, min 40, max 74, median 54.

18 Male recruits, min 19, max 83, median 48.

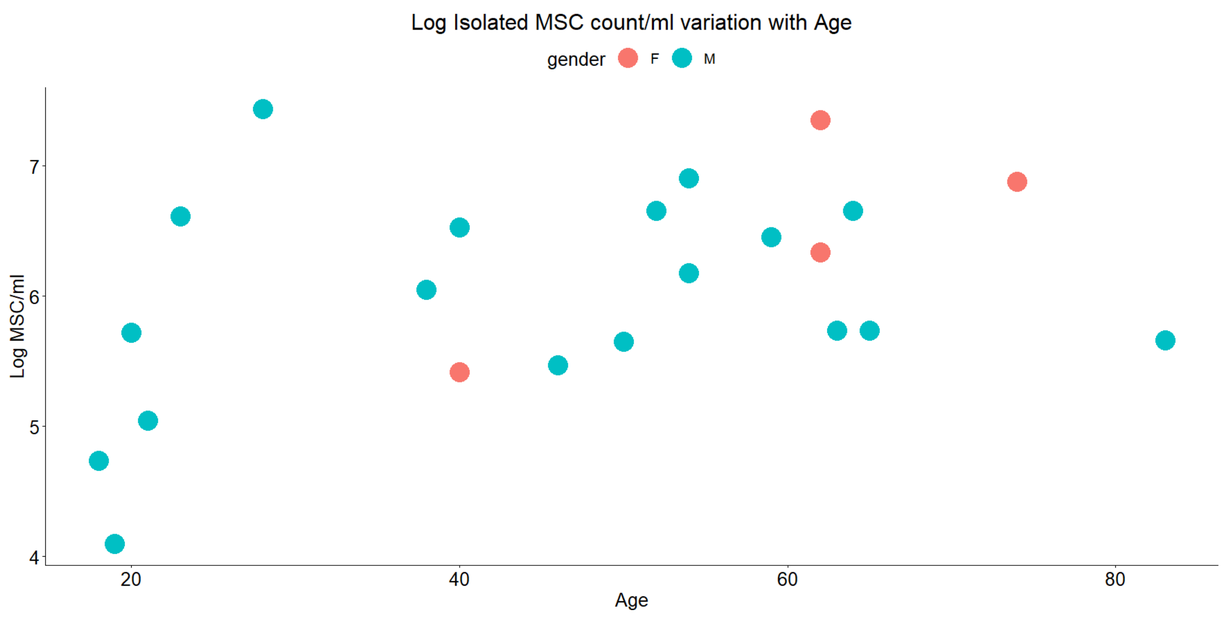


Fig. 2 Log Isolated stem cell concentration variation with age.

The base 10 log of number of stem cells isolated in the sample per unit sample volume.

Discussion

While the recruitment is still on going, some interesting trends are emerging. Many report that the number of stem cells decreases with age but our results to date do not follow that trend for either males or females. Instead the data trends upwards from ages 18 to approximately 35 where it then plateaus, but this does not represent the ability of the cells to replicate or differentiate. Once the data is complete this will be an interesting comparison to make and highlight factors that may shift these counts above and below the trend. Also, of particular interest will be how adipose markers and readings of body composition will relate to osteogenesis.

Further Research

Ultimately this is an exploratory study with the aim to inform future research and develop a tool that help determine a patient's suitability for cell therapy treatments.

Additional sample sites would likely increase the number of participants, but stem cells from other bones sites would be expected to perform differently, this would make for an interesting comparison.

A study using adipocytes as the cells of interesting would provide an interesting contrast of the various influences of the fat / bone axis from the opposite perspective.

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