WINNING ABSTRACTS

3rd place...

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"THE VERTEBRAL BONE MARROW CLOT AS NEW AND ADVANCED AUTOLOGOUS CELL THERAPY IN SPINAL SURGICAL PROCEDURES"

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THE VERTEBRAL BONE MARROW CLOT AS NEW AND ADVANCED AUTOLOGOUS CELL THERAPY IN SPINAL SURGICAL PROCEDURES

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INTRODUCTION

Due to the presence of megakaryocytes, platelets and clotting factors, bone marrow aspirate (BMA) tends to coagulate. For the first time, starting from our previous studies on vertebral mesenchymal stem cells (MSCs)[1], it has been hypothesized that coagulated vertebral BMA (V-BMA) represents a safe and effective autologous biological scaffold for bone regeneration in spinal surgery. The present research involved advanced preclinical *in vitro* models and the execution of a pilot clinical study.

MATERIALS AND METHODS

Evaluation of cell morphology, growth-kinetics, immunophenotyping, clonogenicity, trilineage-differentiation, growth-factors and HOX and TALE gene expression were analyzed on clotted- and un-clotted human V-BMA[2]. In parallel, a pilot clinical study on ten patients with degenerative spine diseases submitted to instrumented posterior arthrodesis, is ongoing to assess the ability of clotted-V-BMA to improve spinal fusion.

RESULTS

Results demonstrated that clotted-V-BMA have significantly higher growth-factor expression and MSCs viability, homogeneity, clonogenicity, and ability to differentiate towards the osteogenic phenotype than un-clotted-V-BMA. Clotted-V-BMA also highlighted significant reduced expression

of PBX1 and of MEIS3 genes negatively involved in osteoblast maturation and differentiation (Fig.1)[1]. From December 2020, six patients have already been enrolled with first promising results that will be finally evaluated in the next 2 months (Fig.2).

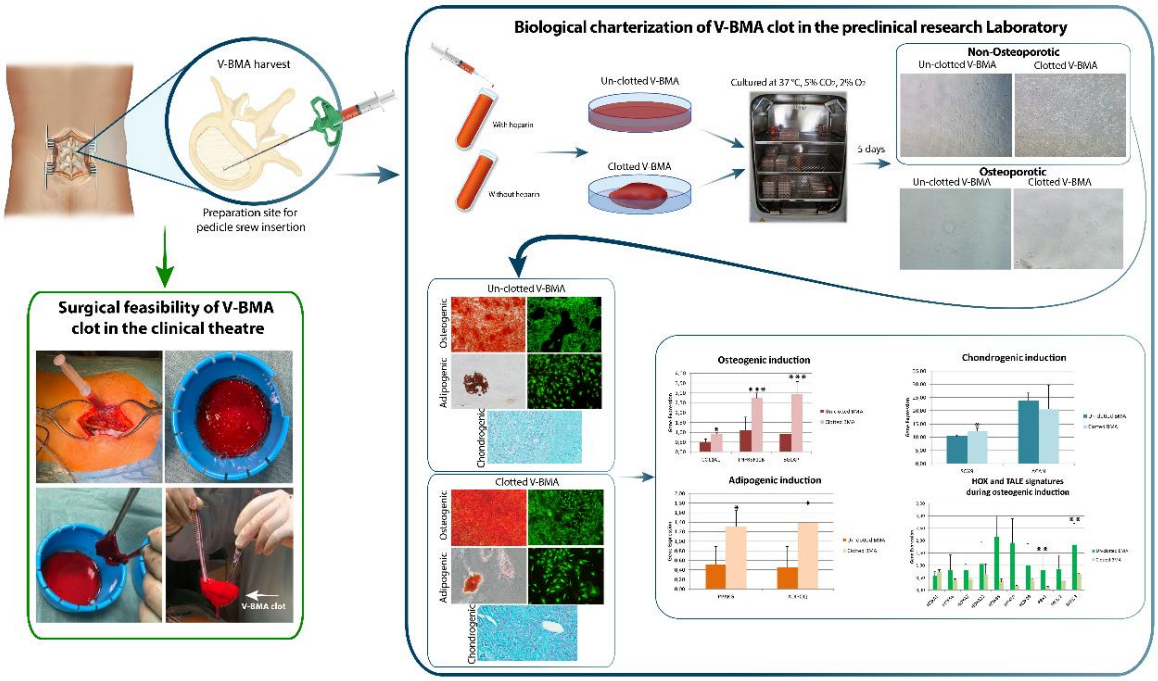

Figure 1: Schematic representation of the preclinical biological characterization of V-BMA clot.

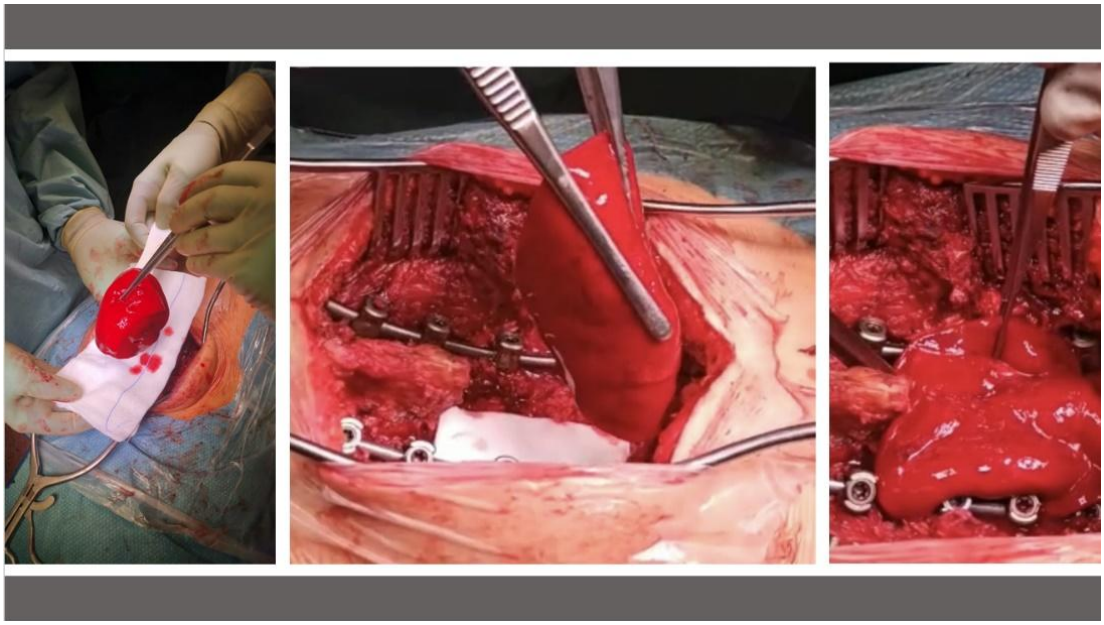

Figure 2: Schematic representation of the clinical procedure employed to use V-BMA clot (Ethics Committee of IRCCS Istituto Ortopedico Rizzoli approval n. CE-AVEC 587/2020/Sper/IOR S).

CONCLUSIONS

The application of V-BMA-clot as carrier of progenitors and cytokines and as natural scaffold with a structural texture represents a point-of-care orthobiologic product to improve spinal fusion. Clinical application seems to be efficacy, and we will confirm and strengthen these data with the results of the pilot clinical study.

REFERENCES

1. Salamanna F, Cepollaro S, Contartese D, Giavaresi G, Brodano GB, Griffoni C, Gasbarrini A, Fini M. Biological Rationale for the Use of Vertebral Whole Bone Marrow in Spinal Surgery. Spine (Phila Pa 1976). 2018 Oct 15;43(20):1401-1410.

2. Salamanna F, Contartese D, Giavaresi G, Sicuro L, Barbanti Brodano G, Gasbarrini A, Fini M. A Rationale for the Use of Clotted Vertebral Bone Marrow to Aid Tissue Regeneration Following Spinal Surgery. Sci Rep. 2020 Mar 5;10(1):4115.

FULL CHARACTERIZATION OF MICROGRAGMENTED ADIPOSE TISSUE: TISSUE ARCHITECTURE, MESENCHYMAL STEM CELL CONTENT AND RELEASE OF PARACRINE MEDIATORS

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INTRODUCTION

The use of microfragmented adipose tissue (mFAT) in different branches of medicine demonstrated positive results in recent case series and clinical trials. This study aims to characterize mFAT in terms of structure, cell content and secreted factors, to evaluate its mechanisms of action.

MATERIALS AND METHODS

Tissue samples (mFAT and lipoaspirate) were collected from 7 donors and tested for:

- Tissue structure (hematoxylin and eosin staining); expression of CD31, CD90, CD146 (immunohistochemistry).
- Expression of CD235a, CD45, CD271, CD105 and senescence (flow cytometry after enzymatic digestion).
- Release of paracrine mediators in conditioned medium (proteomics and miRNomics analyses).
- Tissue composition (proteomics analysis).

RESULTS

Microfragmentation preserves tissue structure while reducing of blood elements. A -76% of erythrocytes and -79% lymphocytes were found in mFAT compared to LA. Senescence was limited in all samples (<5%). Released miRNAs were similar between mFAT and LA, where 381 and 376

different elements were identified, respectively. mFAT and LA conditioned media differ in content of 217 proteins, with processing reducing acute phase elements. Tissue proteomic analyses showed a reduction of extracellular matrix and blood components in mFAT compared to LA.

CONCLUSIONS

These results suggest that mFAT maintains tissue structure and content of Mesenchymal Stem Cells of LA, while it lacks possible detrimental agents such as inflammatory mediators derived from blood (erythrocytes, lymphocytes, acute phase proteins). Then, microfragmentation process represents a safe and efficient method for the application of Mesenchymal Stem Cells properties in Regenerative Medicine.

1st place...

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"DEVELOPMENT OF A MICROFLUIDIC ARTHRITIC JOINT MODEL AS A SCREENING PLATFORM FOR MESENCHYMAL STEM CELL THERAPY"

D. D'Arrigo, D. Petta, C. Arrigoni, L. di Nardo, L. Bonetti,
L. Deabate, C. Candrian, S. Lopa, M. Moretti

DEVELOPMENT OF A MICROFLUIDIC ARTHRITIC JOINT MODEL AS A SCREENING PLATFORM FOR MESENCHYMAL STEM CELL THERAPY

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INTRODCUTION

Osteoarthritis (OA) treatment is hampered by the lack of effective therapeutic treatments and preclinical models whereby new candidate therapies can be evaluated. Our aim is the development of a patient-specific microfluidic model of an arthritic joint, including chondrocytes and synovial fibroblasts, embedded in relevant hydrogels. We used the model to evaluate and compare the anti-inflammatory effect of adipose and bone-marrow mesenchymal stem cells (MSCs).

MATERIALS AND METHODS

We tested hydrogels based on hyaluronic acid (HA) and crosslinked enzymatically or via UV light, evaluating biocompatibility and phenotype of embedded patient-matched fibroblasts and chondrocytes. We optimized the OA microenvironment by adding synovial fluid within the device, and finally we assessed the adipose and bone-marrow MSCs anti-inflammatory capabilities.

RESULTS

Within the enzymatically crosslinked HA-based hydrogel chondrocytes showed a higher viability,

associated to a chondrogenic phenotype. The synovial fluid affected cell viability and morphology. The device also allowed the injection of different MSCs, mimicking an intra-articular injection, and the assessment of their effect on cartilage-like and synovium-like environments.

CONCLUSION

We developed an innovative and patient-specific model of arthritic joint that allows the evaluation and the comparison of different innovative biological OA treatments, such as different MSCs types and their secretome.