

Harnessing the beneficial effects of mesenchymal stem cells during liver machine perfusion: feasibility of an advanced perfusion system coupled with a bioreactor

Alessandra Bertacco¹, Caterina Lonati², Enrico Gringeri¹, Alberto Elmi³, Lucrezia Magnini², Lara Borsetto¹, Maria Laura Bacci³, Francesco Dazzi⁴, Daniele Dondossola², Umberto Cillo¹

¹Hepatobiliary surgery and liver transplant center, 35018, Padua Italy; ²Center for Preclinical Research, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy ³Department of Veterinary Medical Sciences, Bologna, Italy; KHP Lead for Cellular Therapies King's College London, Londra, United Kingdom⁴

Background

NMP could serve as a platform for treatment of marginal livers. Ex-situ administration of mesenchymal-stem-cells (MSCs) exerted multiple positive effects, but the current strategy to apply cell-based therapies during NMP shows some limitations which can affect their effectiveness. To fully harness MSCs benefits, we developed a perfusion system for liver NMP equipped with a MSCs-bioreactor (MSCs-b). The aim of the study was the feasibility of the integration of a MSCs-bioreactor in NMP.

Bioreactors Selection Criteria

- Material inner diameter
- Active surface
- Fiber porosity
- Fiber layout in the housing
- Minimum/maximum flows

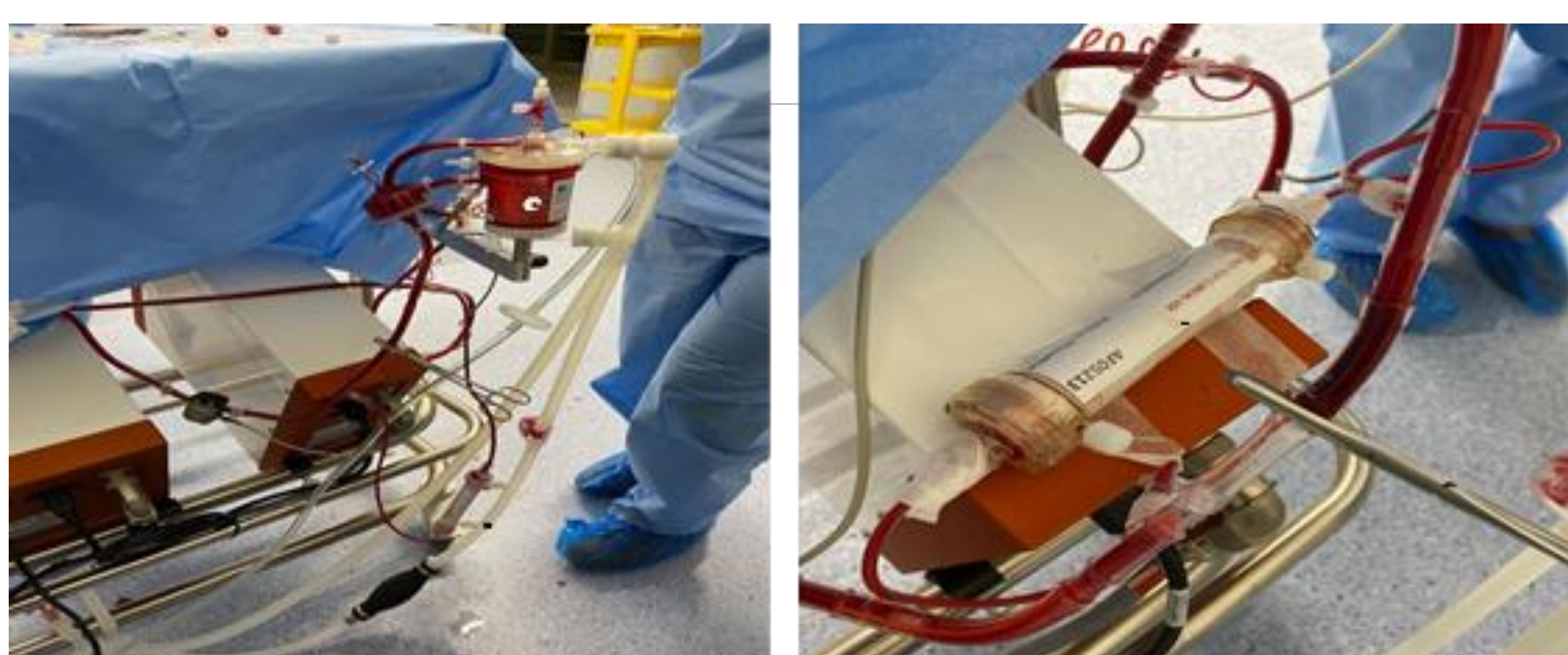


The need of both MSCs cultures on the external side of the fibers and inflammatory mediators and Extracellular vesicle migration to the perfusate towards the organ

Methods

Different models of Polysulfone hollow – fibers were considered for the application with the purpose of having a material allowing MSC licensing factors in the perfusate to activate the MSC in the bioreactor to produce anti-inflammatory molecules which will then be released in the perfusate and reach the liver by means of perfusate recirculation. The assessment was based on: material inner diameter, active surface, fiber porosity, fiber layout in the housing, minimum/maximum flows allowed. MSCs-b was integrated in the NMP system in a close parallel circuit

Results



Rat and pig NMP tests were performed, showing no clotting and no changes in cells vitality and morphology between the start and the end of perfusion.

Characteristics	UM	"Type-1"	"Type-2"
Surface	m ²	0,05	0,075
Inner diameter	μ	300	250
Wall Thickness	μ	85	50
Priming volume (Inner Fibers)	ml	3,9	5
TMP Max	mmHg	100	600
Max Flow	ml/min	20	100
CUT OFF (est)	Da	1,5 Mio	50k

Conclusion

MSCs integration in NMP is feasible and apparently safe for organ perfusion. MSCs seems to express immunomodulatory proprieties.