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Italiadomani
PIANO NAZIONALE DI RIPRESA E RESILIENZA

Innovation, digitalisation and sustainability for the diffused economy in Central Italy

Università degli Studi di Urbino Carlo Bo
17 dicembre 2024

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Advanced drug delivery systems and in vivo theranostic tools for personalised medicine

The main goal of the WP3 is the design of innovative strategies to reach patient-centered therapies personalized on specific patient needs in terms of efficacy, accuracy, safety, and/or compliance of diagnosis and treatment of diseases. To this end, three specific objectives will be pursued:

T3.1 Development of **personalized pharmaceutical dosage forms** by additive manufacturing technologies;

T3.2 Engineering **bioinspired** and **biomimetic nanomedicines** for precise drug delivery;

T3.3 Optimization of **innovative methods to screen tissues and organs** based on drug loaded iron oxide nanoparticles (SPION) and/or gadolinium synthetic derivatives, embedded into red blood cells that can be magnetically guided and traced by Magnetic Resonance Imaging (MRI) and magnetic particle imaging (MPI).

1506 UNIVERSITÀ DEGLI STUDI DI URBINO CARLO BO
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Task	Task Name	People
T3.1	Development of personalized dosage forms by additive manufacturing technologies	**Luca Casettari** **Annalisa Aluigi** Mattia Tiboni
T3.2	Engineering bioinspired and biomimetic nanomedicines for precise drug delivery	**Michele Guescini** (*Silvestri Sonia*) **Barbara Canonico** (*Mariele Montanari*) **Francesca Luchetti** **Piero Sestili** Rossana Rauti Sara Biagiotti
T3.3	Red blood cells as theranostic system for in vivo applications	**Luigia Rossi** **Luca Giorgi** (*Luca Mancini*) Antonella Antonelli

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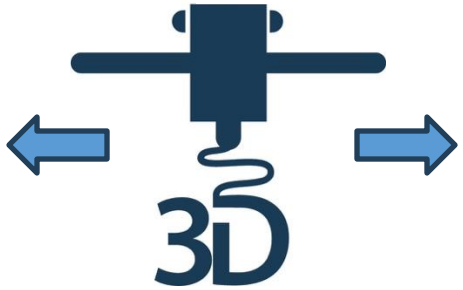
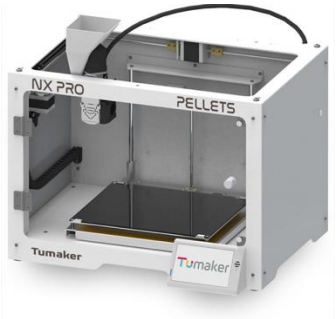
T3.1 Development of personalized dosage forms by additive manufacturing technologies

Personalized Pharmaceutical Formulations



Engineered devices manufacturing & QC



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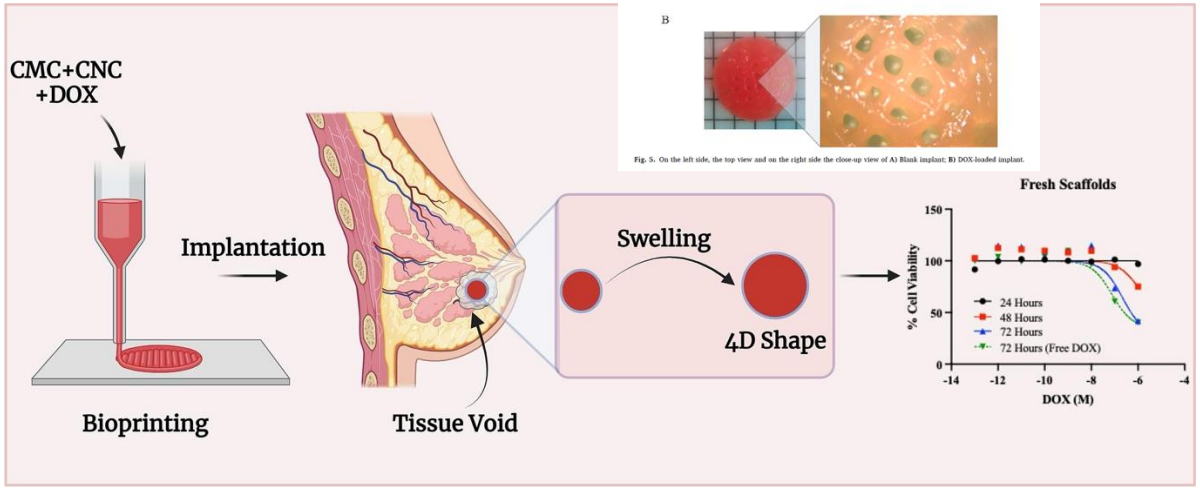
Moroni S., Bingham R., Buckley N., Casettari L. and Lamprou D.A.
4D printed multipurpose smart implants for breast cancer management
International Journal of Pharmaceutics – Volume 642, July 2023



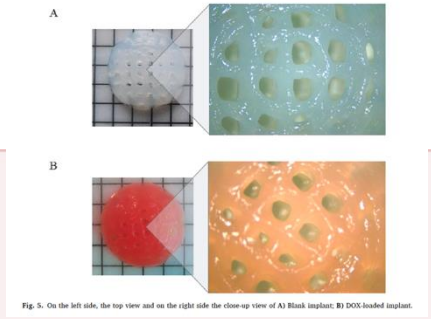
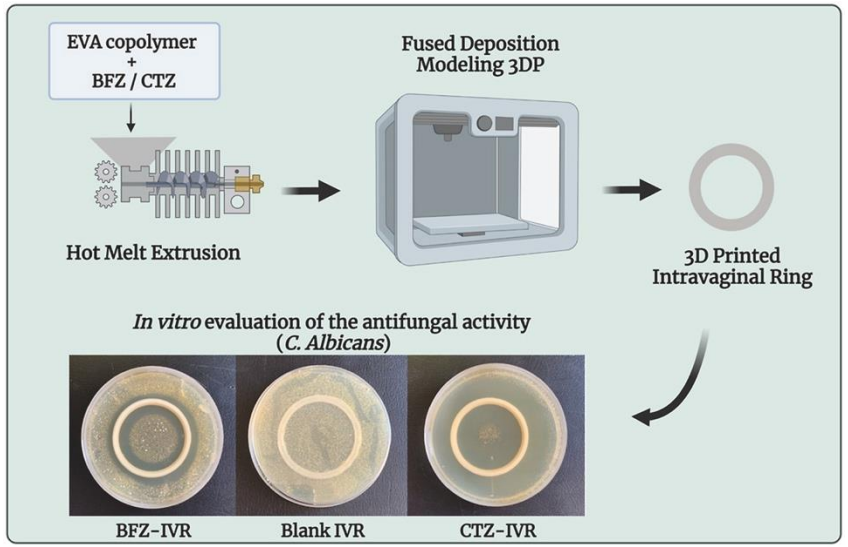
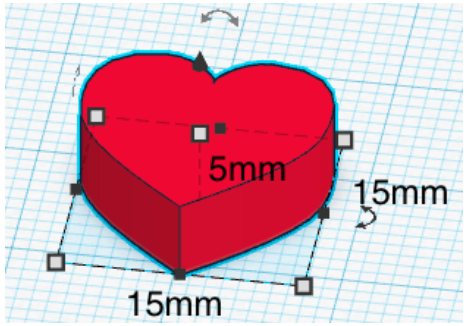
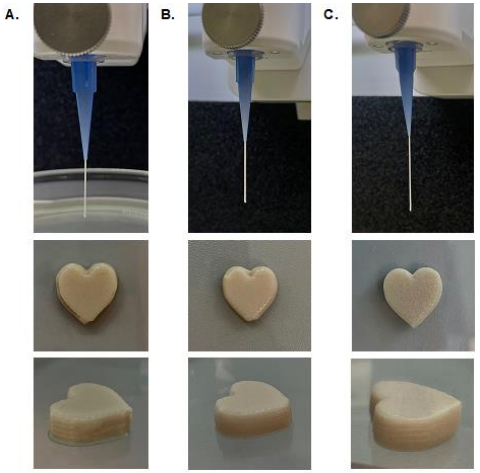
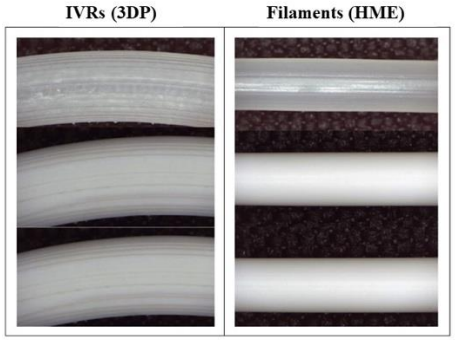


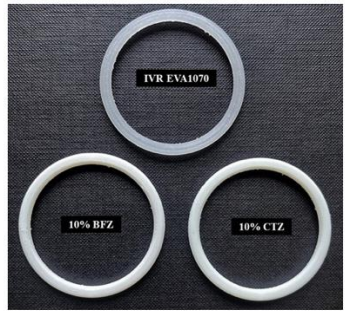
Fig. 5. On the left side, the top view and on the right side the close-up view of A) Blank implant; B) DOX-loaded implant.



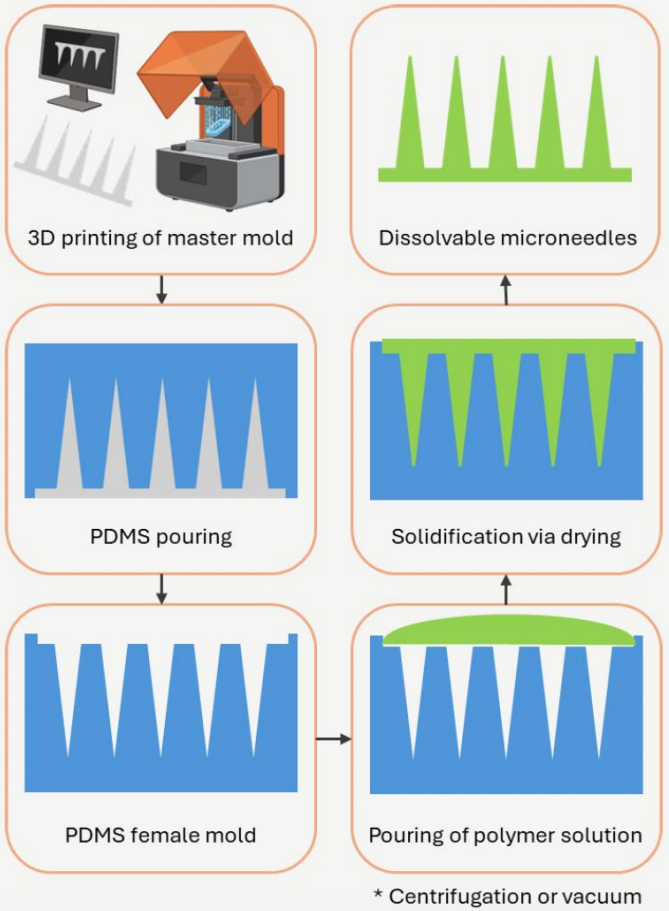


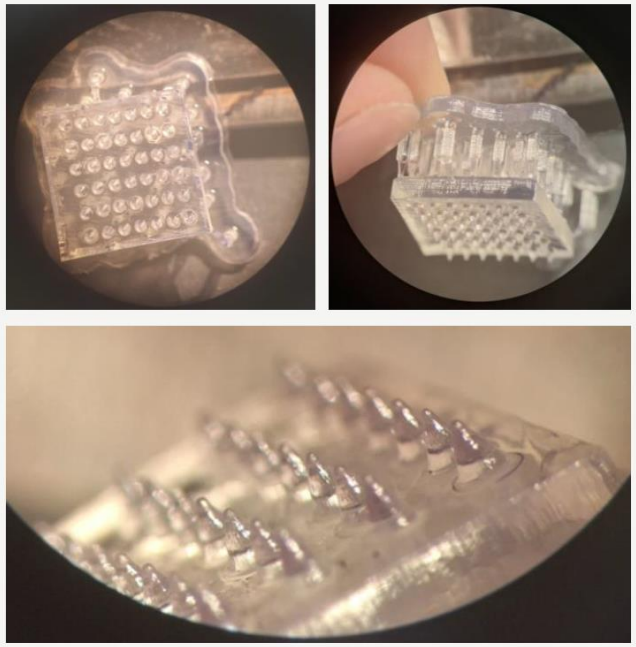


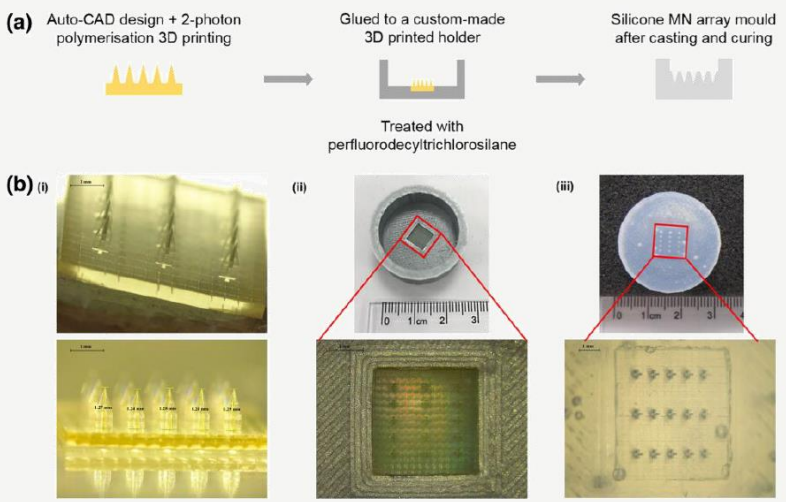


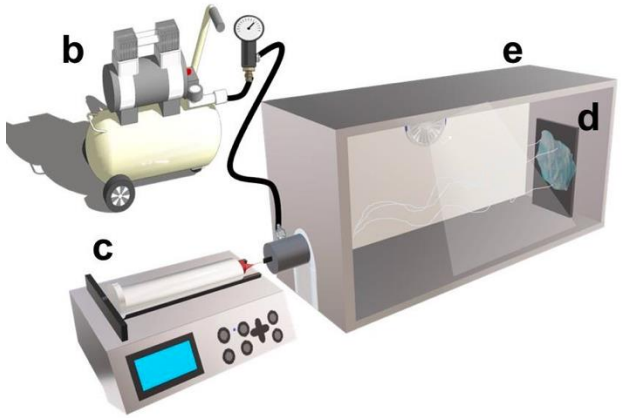


Moroni S., Bischi F., Aluigi A., Campana R., Tiboni M.* and Casettari L.
3D printing fabrication of Ethylene-Vinyl Acetate (EVA) based intravaginal rings for antifungal therapy
Journal of Drug Delivery Science and Technology – Volume 84, June 2023, 104469 2023

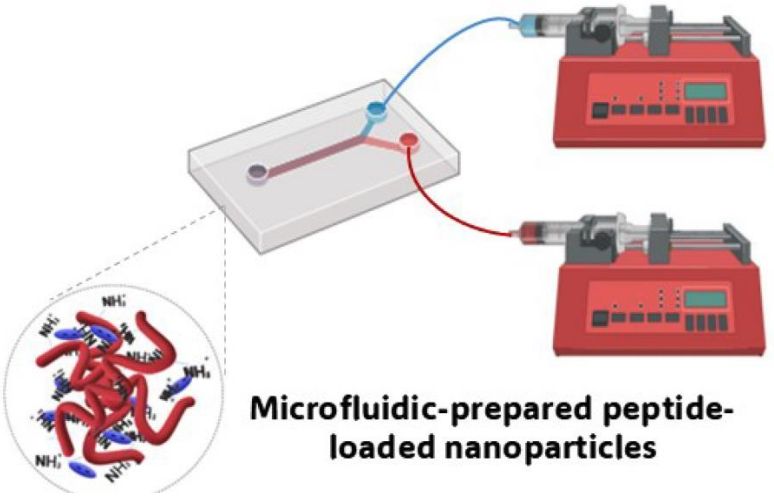

3D printing of master mold
Dissolvable microneedles
PDMS pouring
Solidification via drying
PDMS female mold
Pouring of polymer solution
* Centrifugation or vacuum



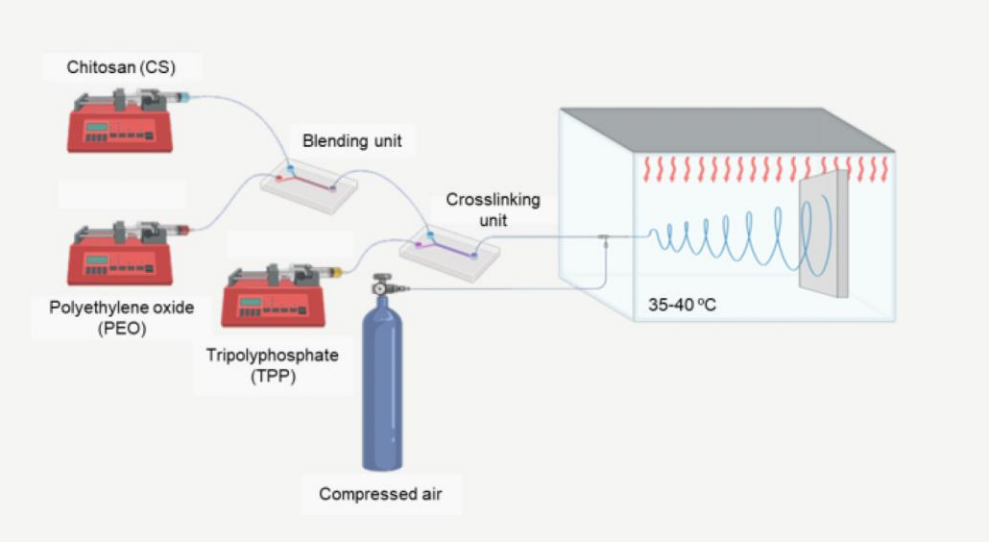

(a)
Auto-CAD design + 2-photon polymerisation 3D printing
Glued to a custom-made 3D printed holder
Silicone MN array mould after casting and curing
Treated with perfluorodecyltrichlorosilane
(b)
(i)
(ii)
(iii)



Maurizii G., Valentini L., Sotgiu G., Zamboni R., Tonetti C., Vineis C., Canonico B., Montanari M., Tiboni M., Casettari L. and Aluigi A.*
The dark side of the wool? From wool wastes to keratin microfilaments through the solution blow spinning process
International Journal of Biological Macromolecules – Volume 275, Part 2, August 2024, 133722



Maurizii G., Moroni S., Jimènez Núnez J.V., Curzi G., Tiboni M., Aluigi A. and Casettari L.*
Non-invasive peptides delivery using chitosan nanoparticles assembled via scalable microfluidic technology
Carbohydrate Polymer Technologies and Applications – Volume 7, June 2024, 100424



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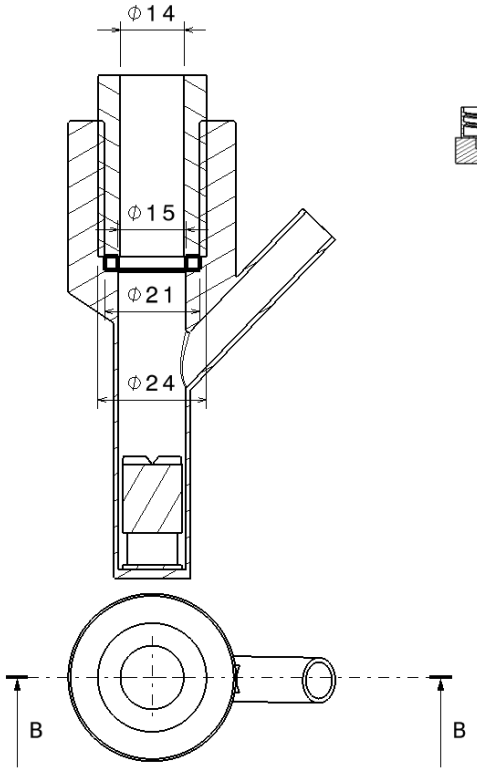

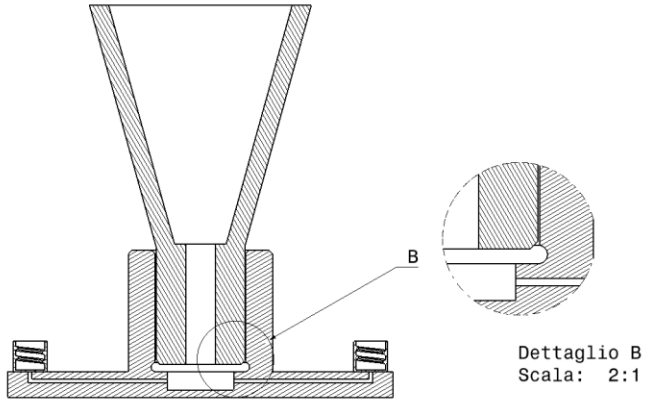

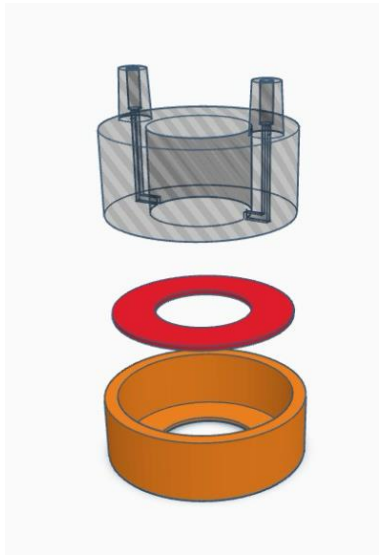

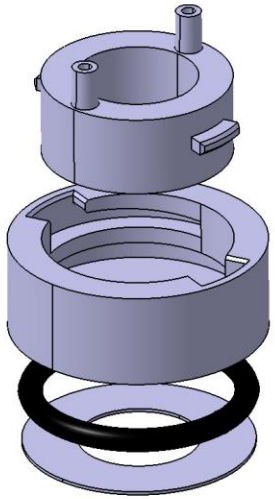

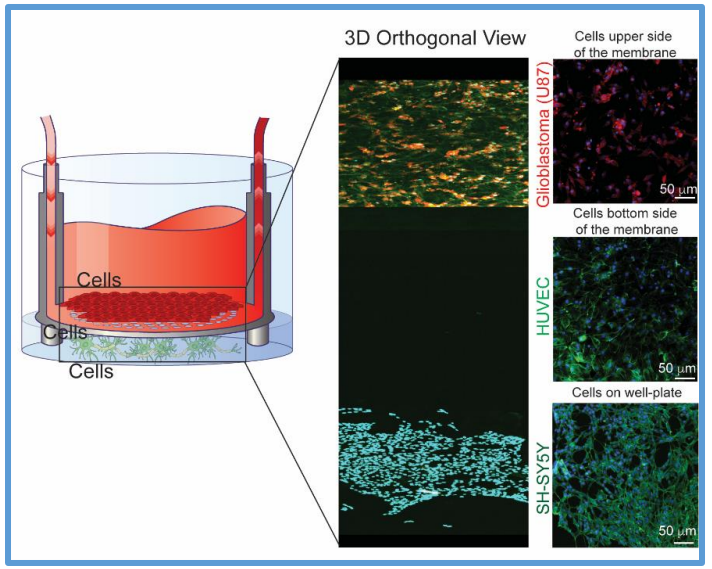

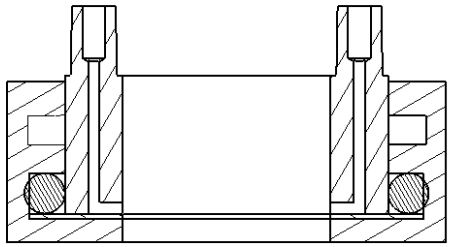

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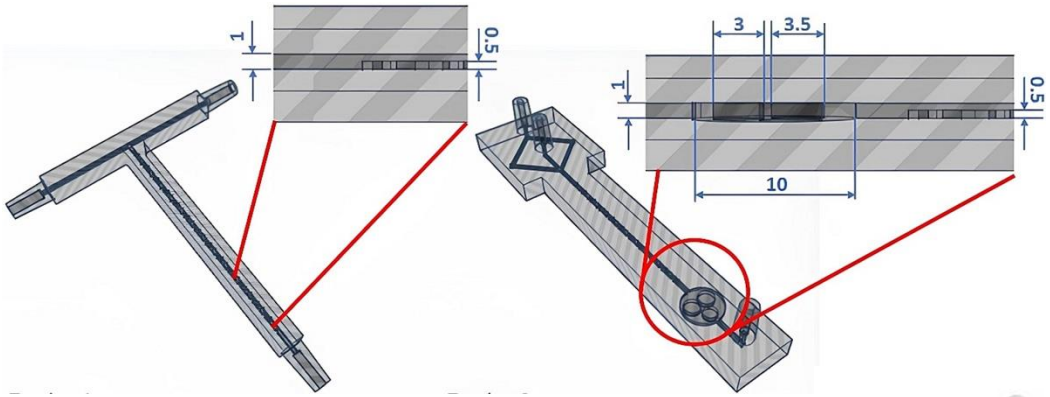
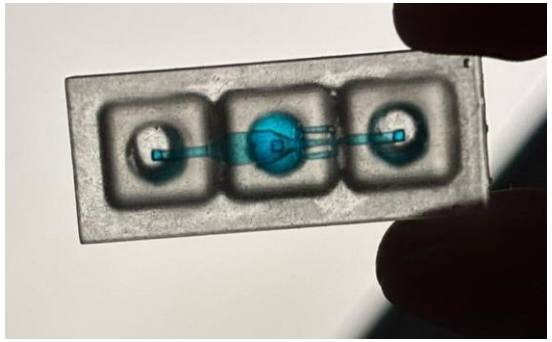
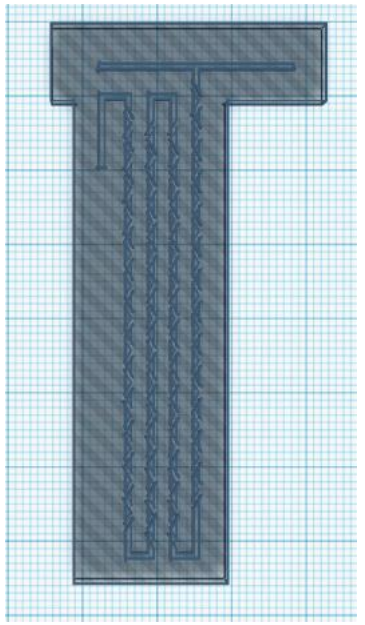
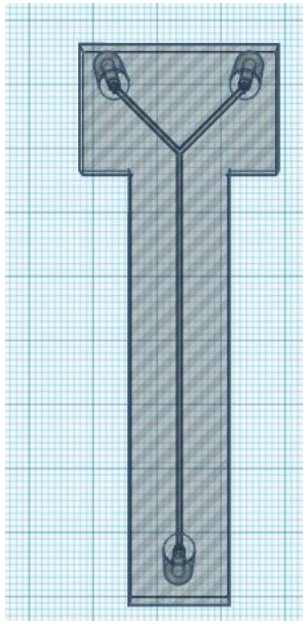
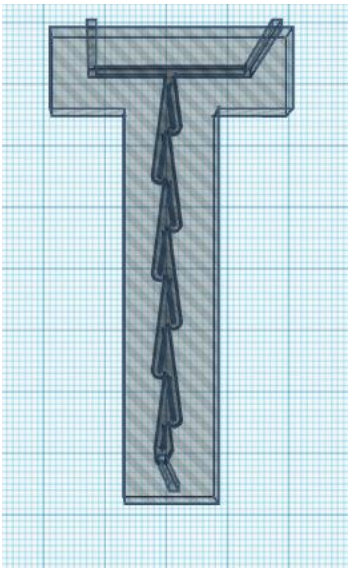
T3.2 Engineering bioinspired and biomimetic nanomedicines for precise drug delivery











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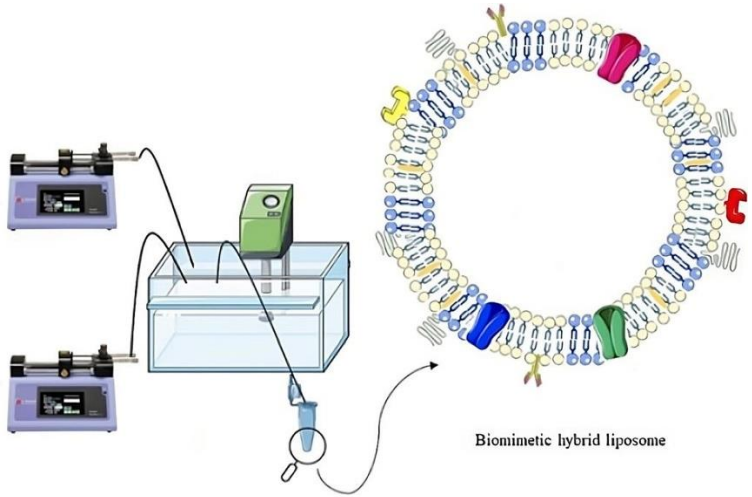
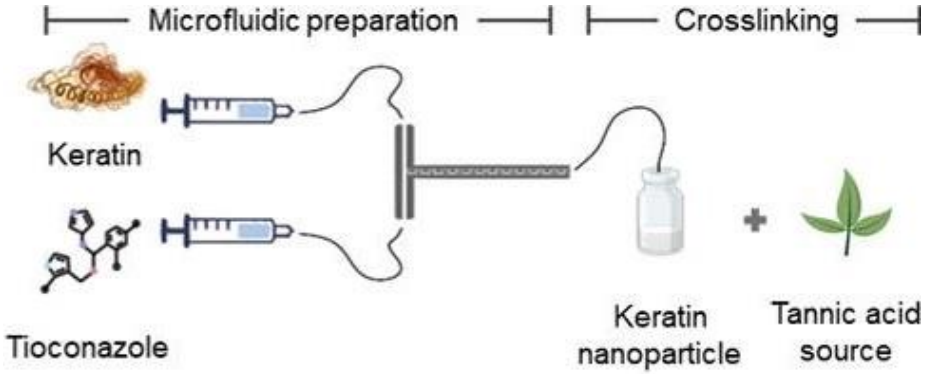
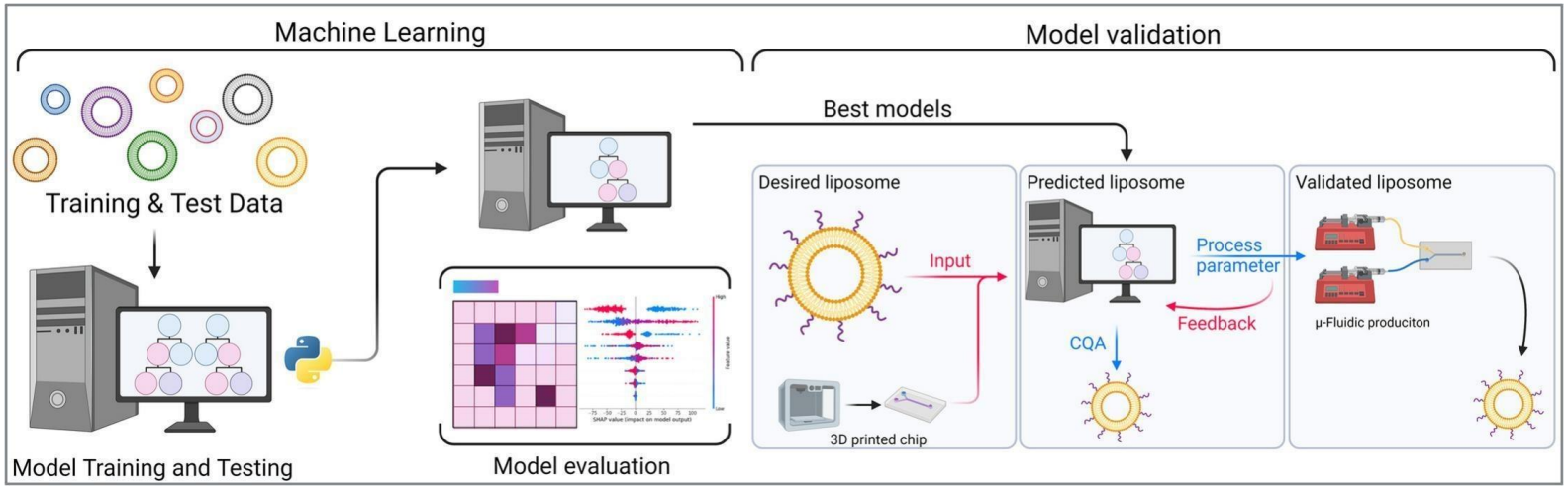




Khorshid S., Goffi R., Maurizii G., Benedetti S., Sotgiu G.*, Zamboni R., Buoso S., Galuppi R., Bordoni T., Tiboni M., Aluigi A.* , Casettari L.
Microfluidic manufacturing of Tioconazole loaded keratin nanocarriers: development and optimization by Design of Experiments
International Journal of Pharmaceutics – Volume 647, 25 November 2023, 123489



Eugster R., Orsi M., Buttitta G., Serafini N., Tiboni M., Casettari L., Reymond J.L., Aleandri S., and Luciani P.*
Leveraging machine learning to streamline the development of liposomal drug delivery systems
Journal of Controlled Release – Volume 376, December 2024, Pages 1025-1038

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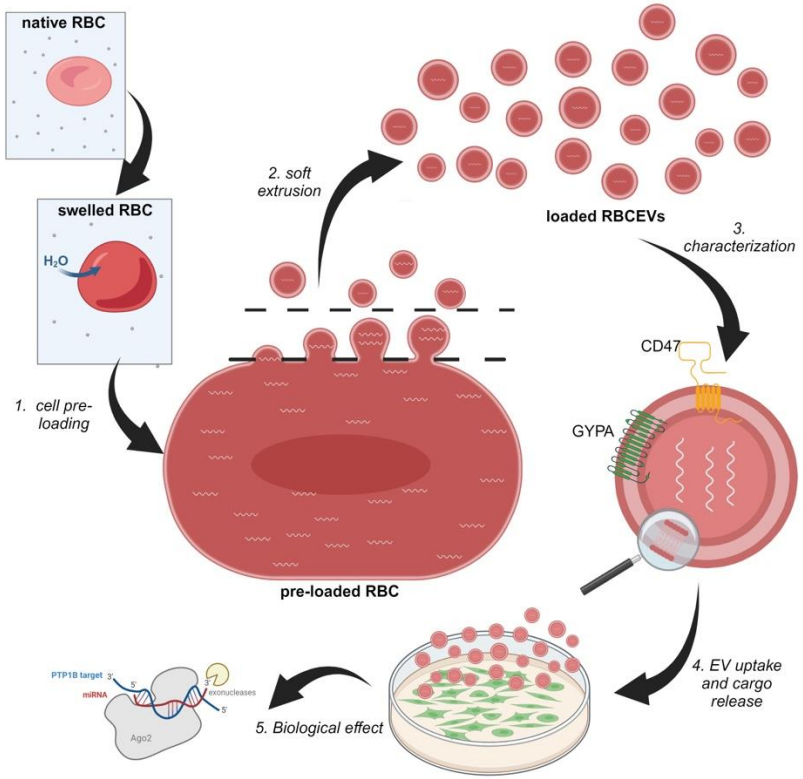
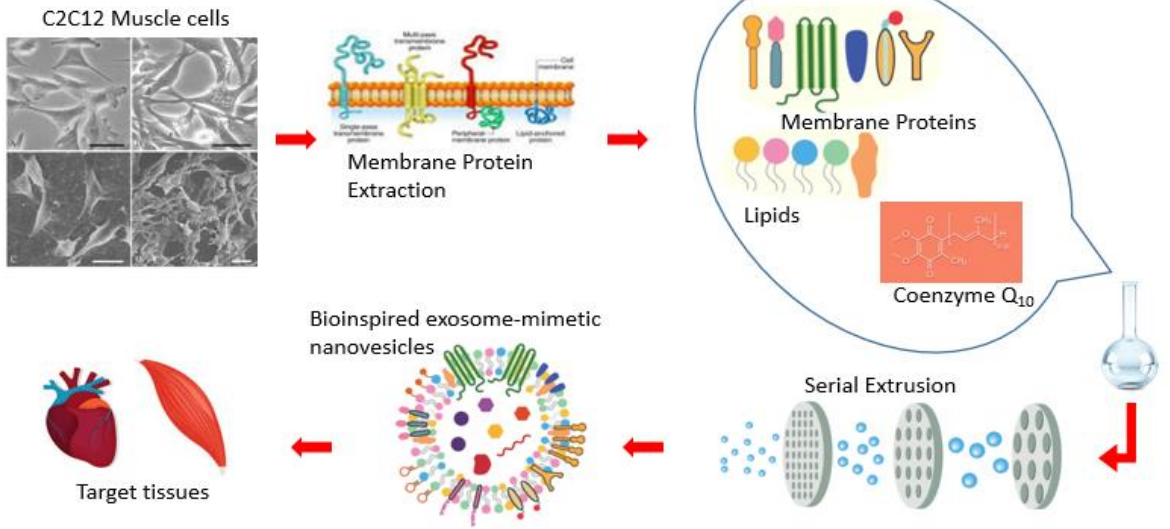
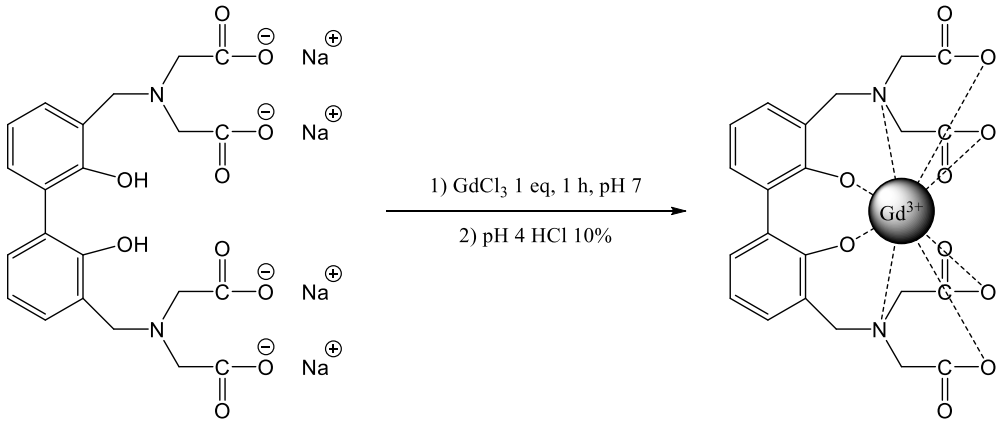




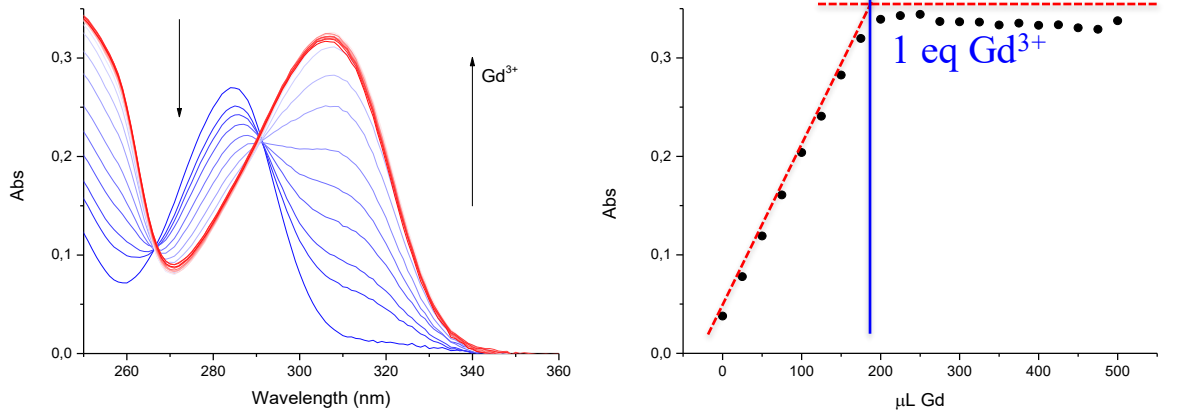
Biagiotti S.*, Canonico B., TiboniM., Abbas F., Pirla E., Montanari M., BattistelliM., Papa S., Casettari L., Rossi L., Guescini M. and Magnani M.
Efficient and highly reproducible production of red blood cells-derived extracellular vesicle mimetic for the loading and delivery of RNA molecules
Scientific Reports – *14:14610* – 2024

Patent application n. 102023000026244
RBCs-derived Extracellular Vesicles Loaded with Cargo Molecules for Therapeutic Applications and Method of Production Thereof

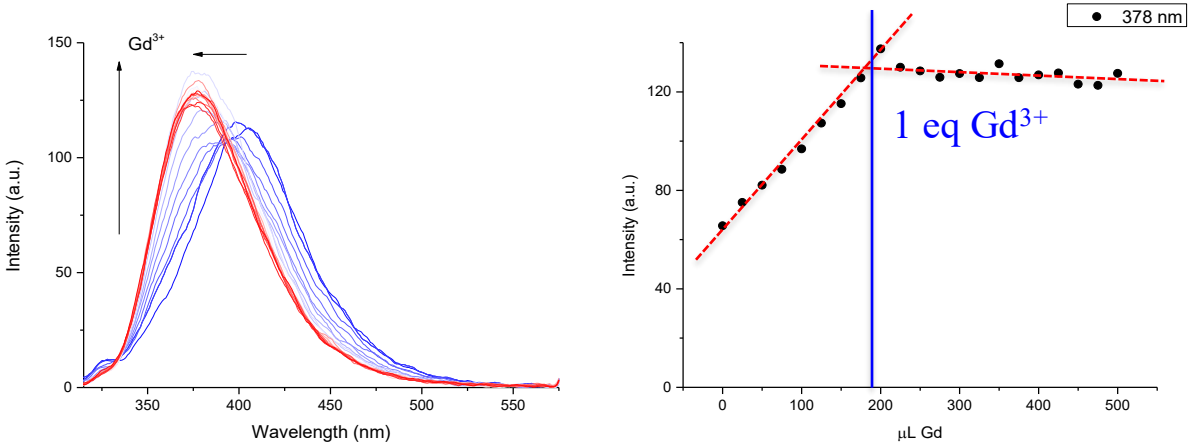
T3.3 Red blood cells as theranostic system for in vivo applications



Titolazione UV-Visibile



Titolazione in Fluorescenza



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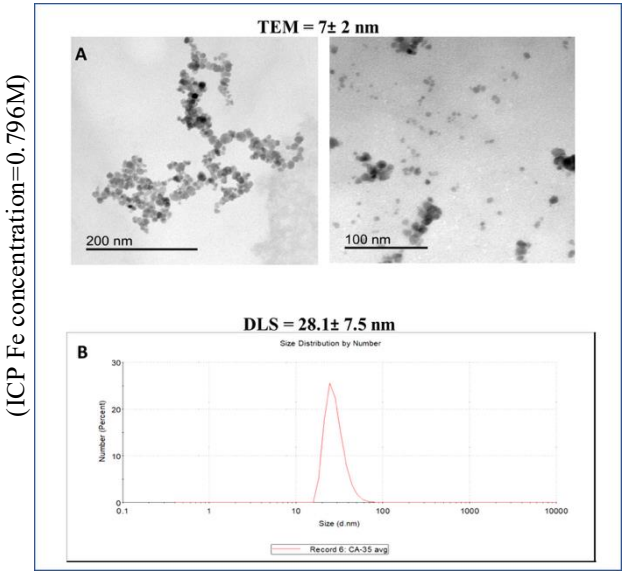
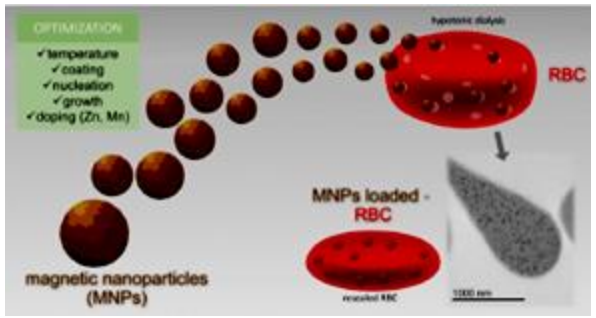
Optimization of SPIOs nanoparticle synthesis to optimally and ideally load into red blood cells (RBCs)

Transmission Electron Microscope (TEM) image of CA-35 DX nanoparticles (**A**) and their size distribution with Dynamic Light Scattering (DLS) (**B**)

CA-35DX iron oxide suspension (ICP Fe concentration=0.796M)

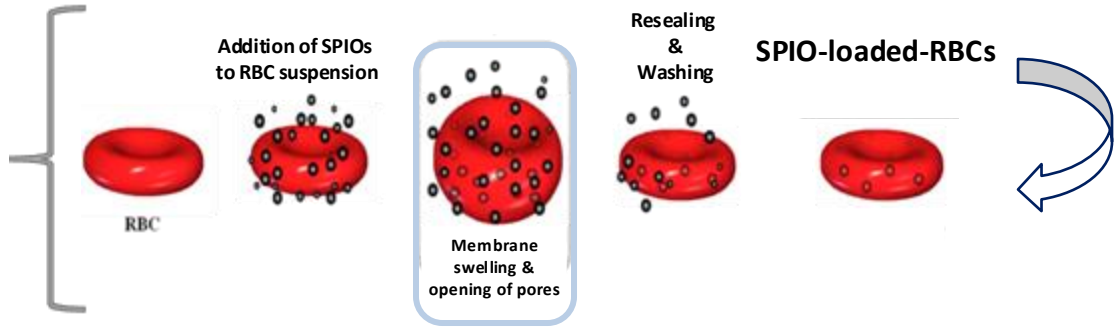


focus



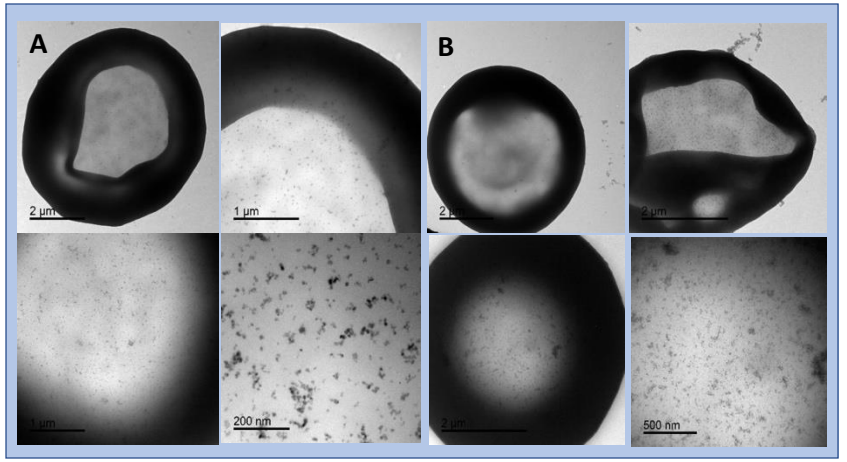
How to transform a Red Blood Cell into a carrier

....starting from controlled blood sample



RESULTS

Transmission Electron Microscope (TEM) analyses of whole human CA-35DX-Loaded RBCs **A**) CA-35 DX-L3-RBCs, **B**) CA-35 DX-L4-RBCs



NMR measurements of T1 and T2 values of human CA-35 DX-loaded RBCs prepared by using different Fe amounts (from 2.8 mg to 22.4 mg Fe) during loading procedure schematically above reported

Samples	HCT (%)	Peak intensity T1 (ms)	Peak intensity T2 (ms)	Peak area T1 (ms)	Peak area T2 (ms)	[mM Fe] *vs UL-RBCs (r1=1.1523)*
ND-RBCs	44	2325	64.74	2166	72	/
UNLOADED-RBCs	44	1932	43.55	1841	43.1	/
L1-CA-35 DX-RBCs	43	335.57	<5	302.65	<5	**2.2**
L2-CA-35 DX-RBCs	43	223.66	/	199.22	5	**3.5**
L3-CA-35 DX-RBCs	44	100.71	<5	96.33	/	**8.3**
L4-CA-35 DX-RBCs	45	57.60	/	/	/	**14.7**

Grazie per l'attenzione