

# Nanomedicine and Nanoscale Delivery I

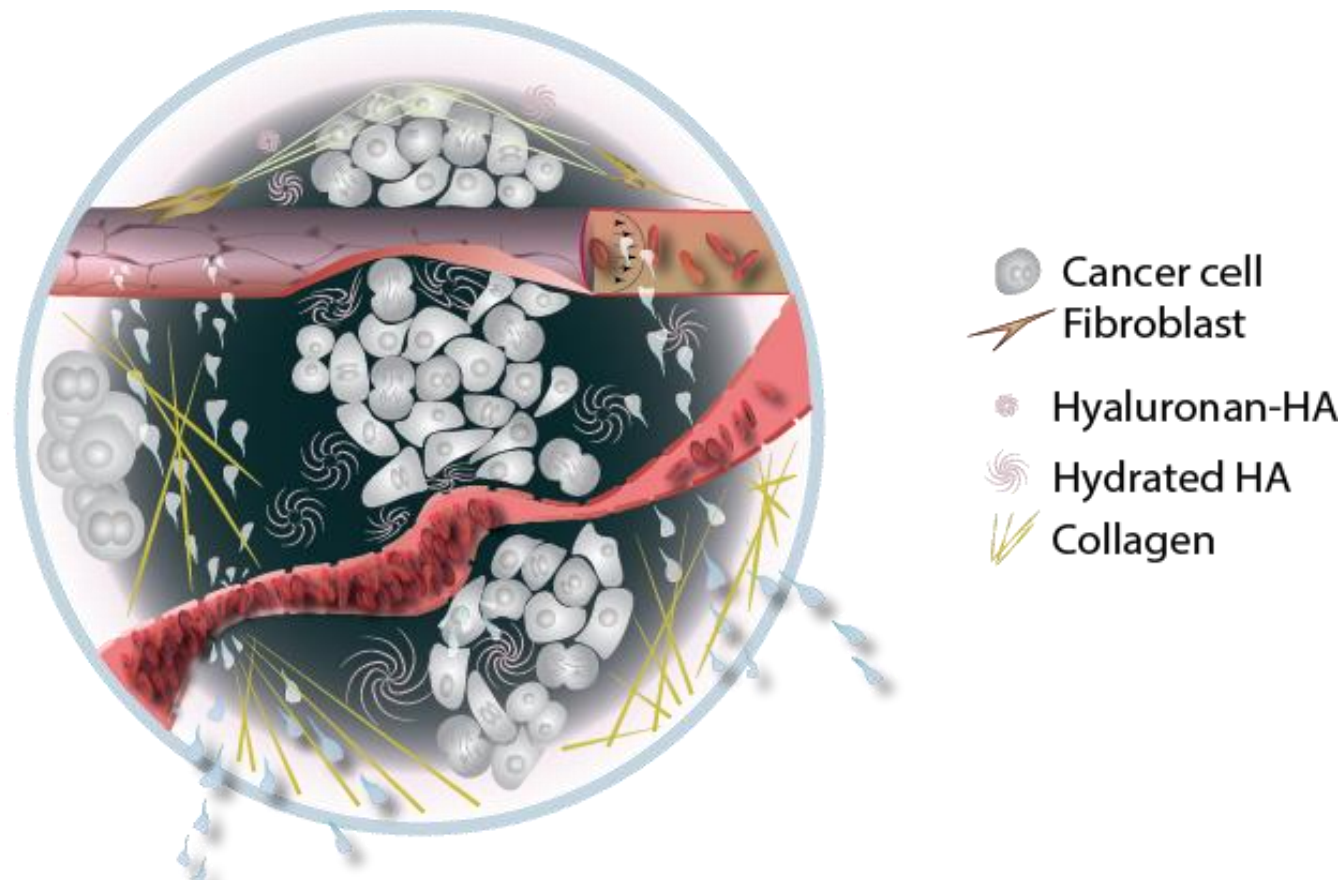
Combining two strategies to modulate the tumor microenvironment and optimize efficacy of nano-immunotherapy

Fotios Mpekris

Research Assistant Professor  
University of Cyprus



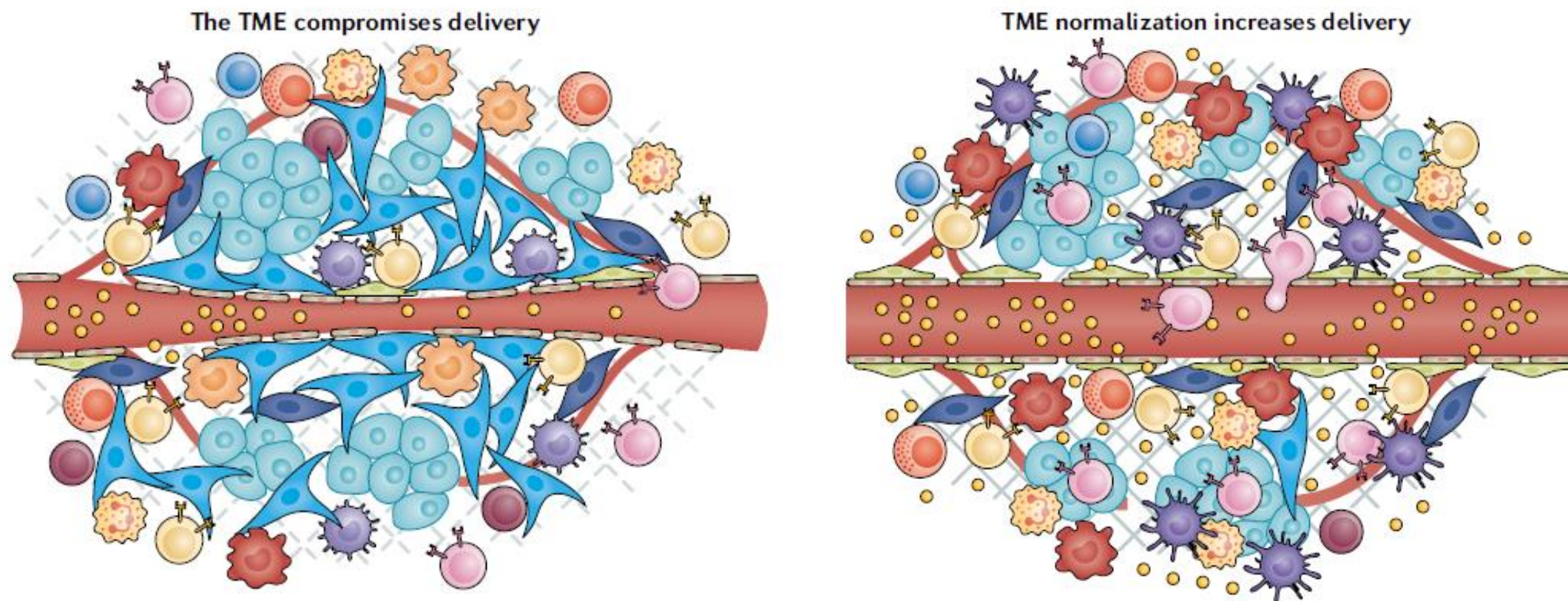
# The tumor mechanical micro-environment



Stylianopoulos et al., Trends in Cancer, 2018



# Re-engineering Cancer



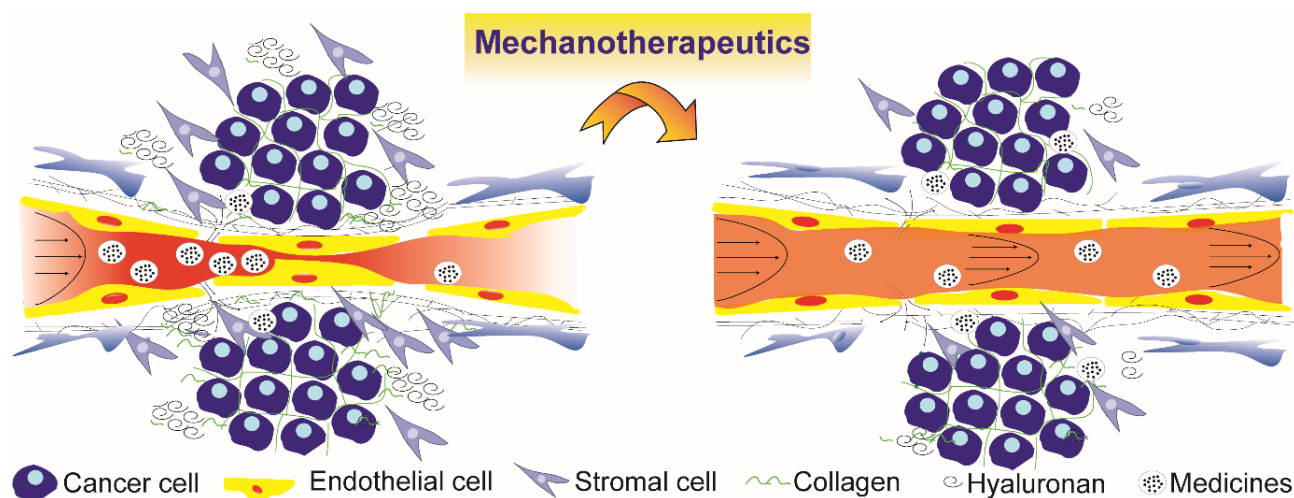
Martin JD, et al, Nature Reviews Clinical Oncology, 2020



# The promise of mechanotherapeutics and sonopermeation

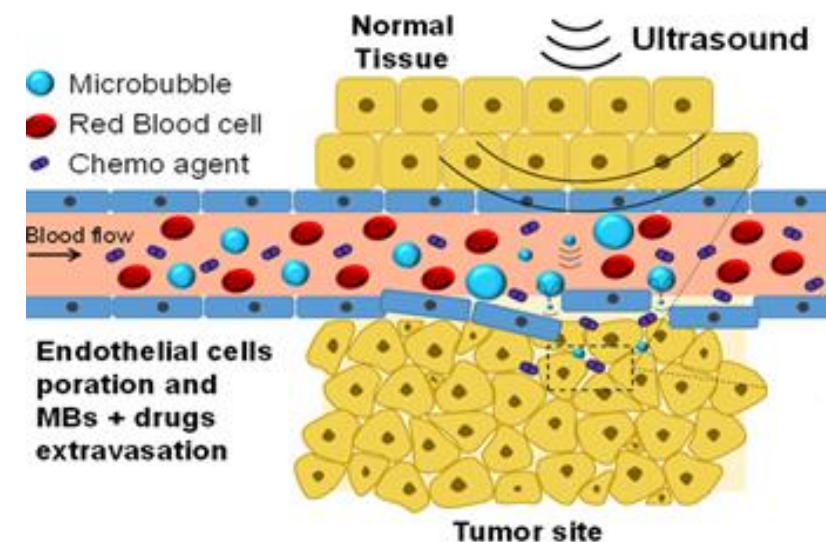
## Mechanotherapeutics

- ✓ Modulate mechanical forces in tumors
- ✗ Can decompress only a 40% of the vessels

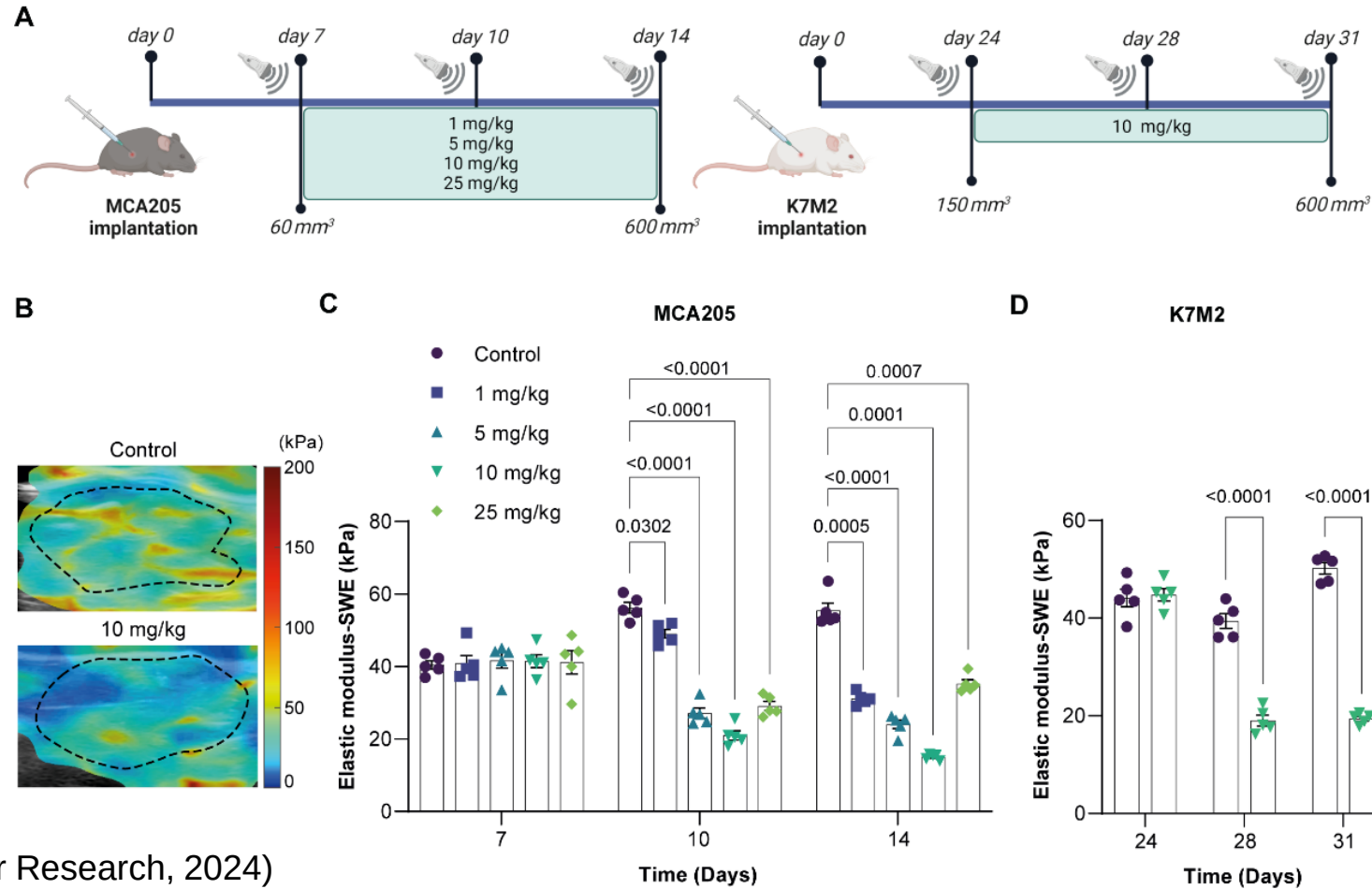


## Sonopermeation

- ✓ Enhance tumor perfusion non-invasively
- ✗ Collapsed vessels cannot deliver Microbubbles



# Ketotifen decrease mechanical forces



(Panagi M. et al, Clinical Cancer Research, 2024)



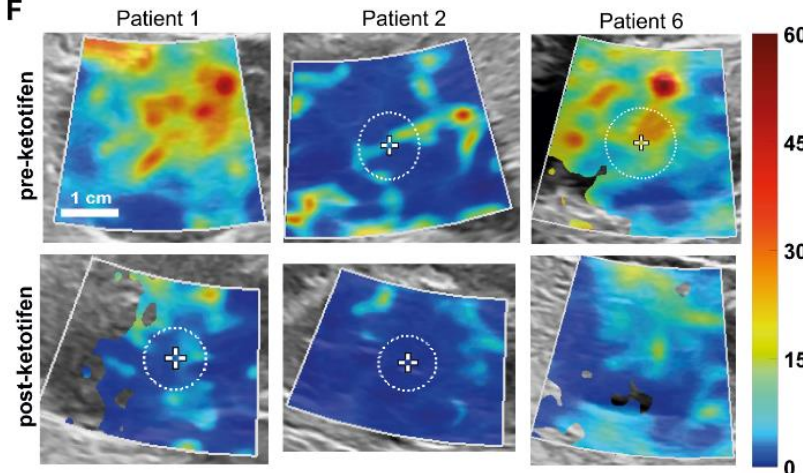
# Ketotifen decrease mechanical forces

E

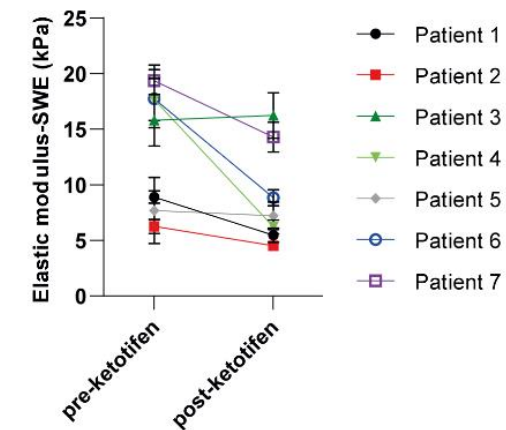
| Demographics and clinical characteristics |                            |     |        | SWE                      |                                |                           |                      |
|-------------------------------------------|----------------------------|-----|--------|--------------------------|--------------------------------|---------------------------|----------------------|
|                                           | Diagnosis                  | Age | Gender | Baseline stiffness (kPa) | Post-ketotifen stiffness (kPa) | Treatment duration (days) | p value <sup>a</sup> |
| Patient 1                                 | Epithelioid leiomyosarcoma | 70  | F      | 8,90                     | 6,70                           | 123                       | <b>0,026</b>         |
| Patient 2                                 | Myxofibrosarcoma           | 66  | F      | 6,26                     | 4,50                           | 155                       | <b>0,048</b>         |
| Patient 3                                 | Atypical lipomatous tumor  | 62  | F      | 15,80                    | 16,23                          | 8                         | 0,890                |
| Patient 4                                 | Leiomyosarcoma             | 69  | M      | 17,66                    | 6,21                           | 140                       | <b>1,5E-04</b>       |
| Patient 5                                 | Pleomorphic leiomyosarcoma | 47  | F      | 7,68                     | 7,21                           | 8                         | 0,881                |
| Patient 6                                 | Synovial sarcoma           | 79  | M      | 17,74                    | 8,835                          | 55                        | <b>0,006</b>         |
| Patient 7                                 | Desmoid tumor              | 31  | F      | 19,36                    | 14,29                          | 7                         | <b>0,020</b>         |

<sup>a</sup> P values are from non-parametric T-test, significant p values are in bold

F

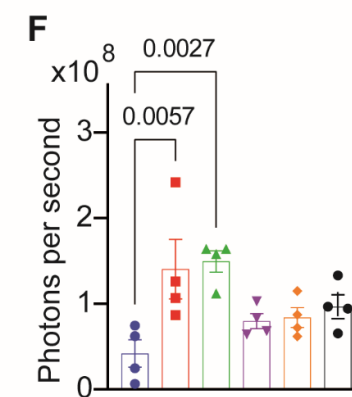
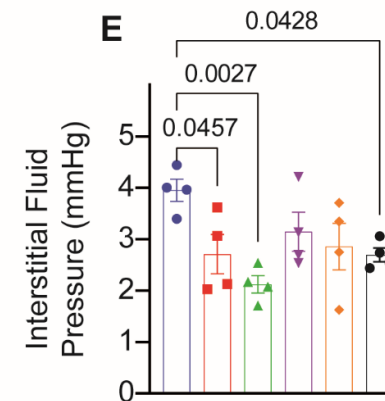
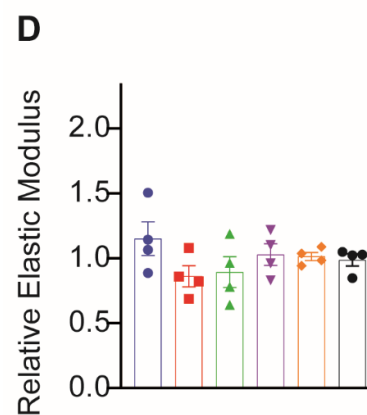
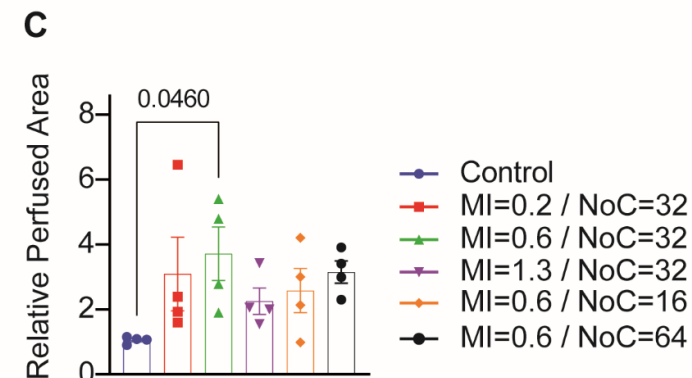
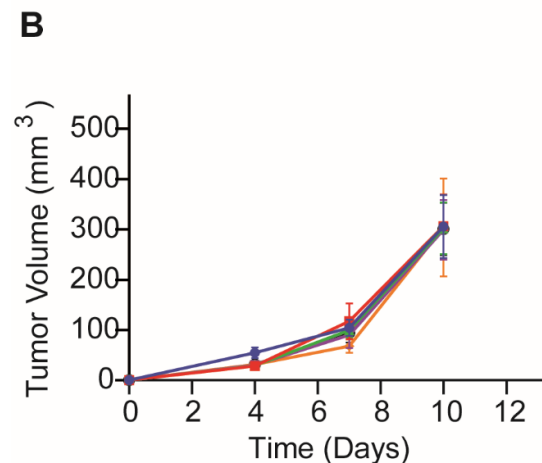
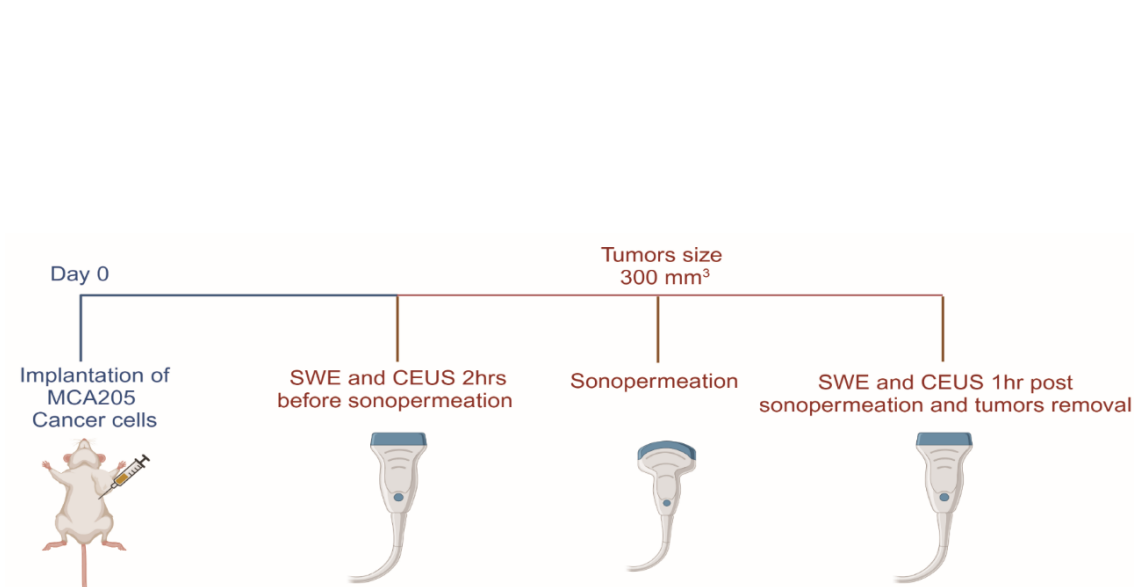


G



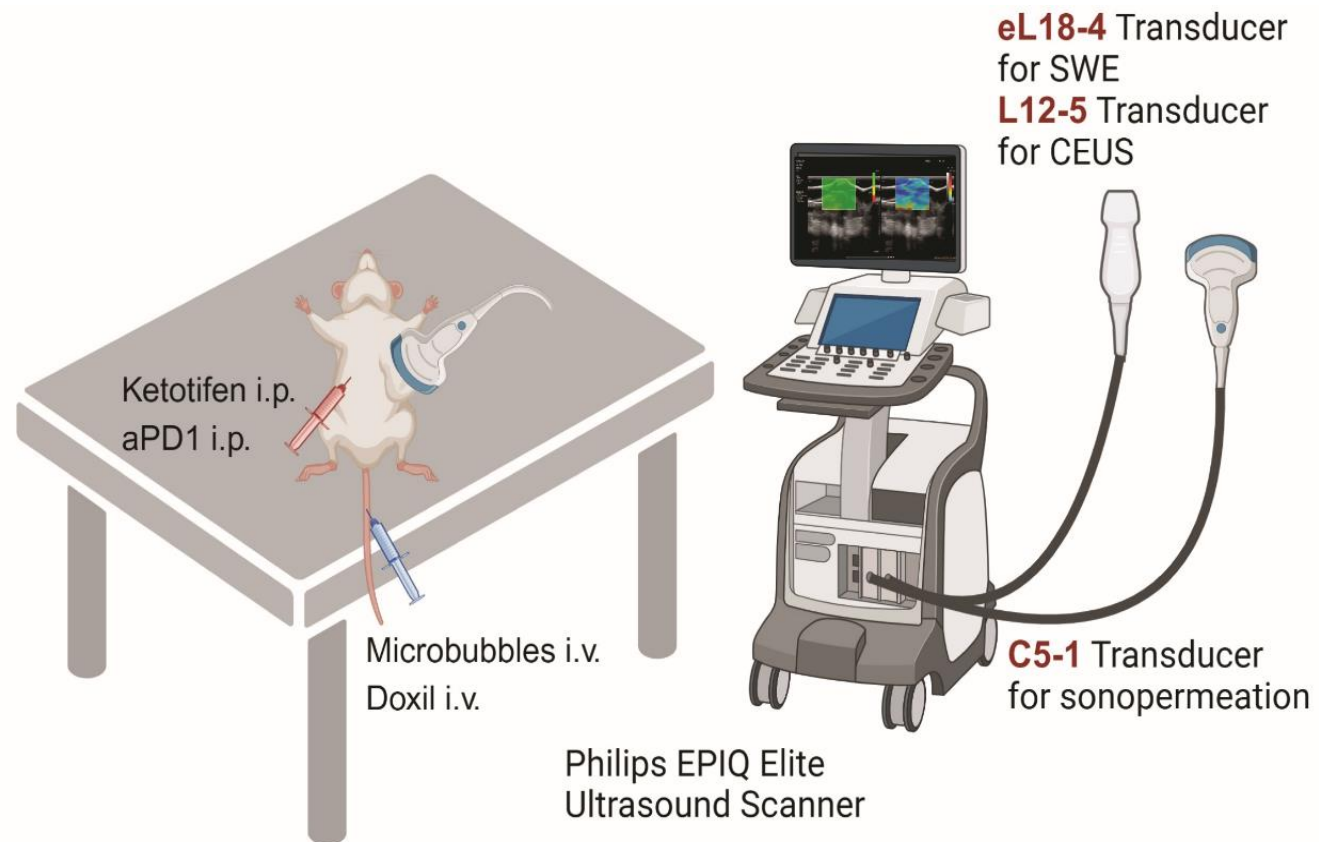
(Panagi M. et al, Clinical Cancer Research, 2024)

# Sonopermeation improves tumor perfusion



Mpekris F. et al, Neoplasia, 2024

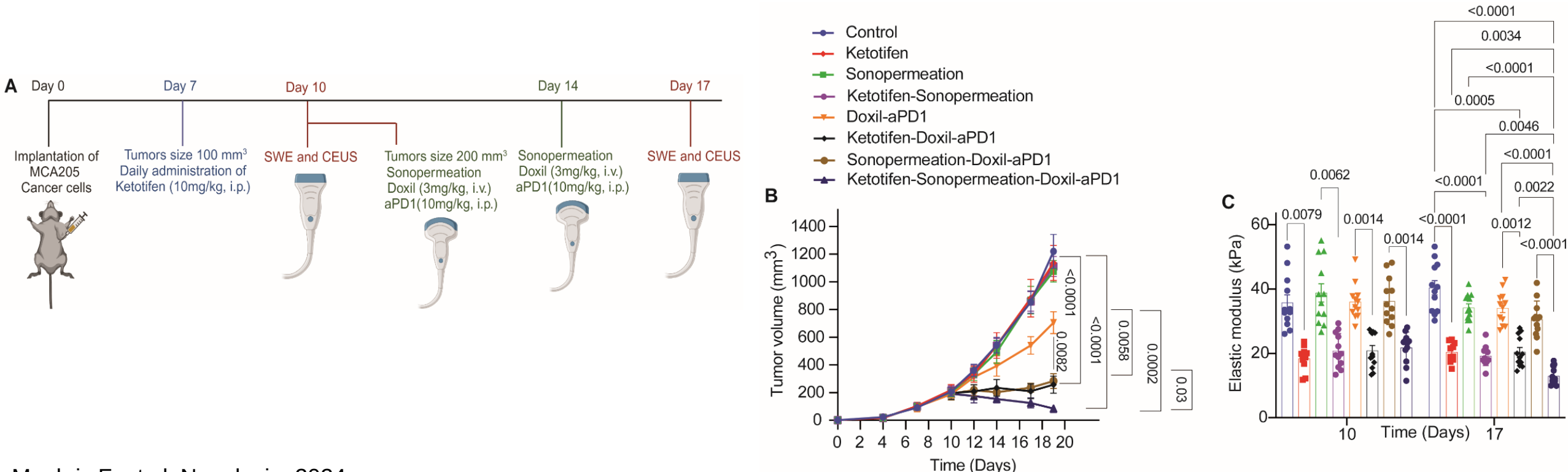
# Experimental setup



Mpekris F. et al, Neoplasia, 2024

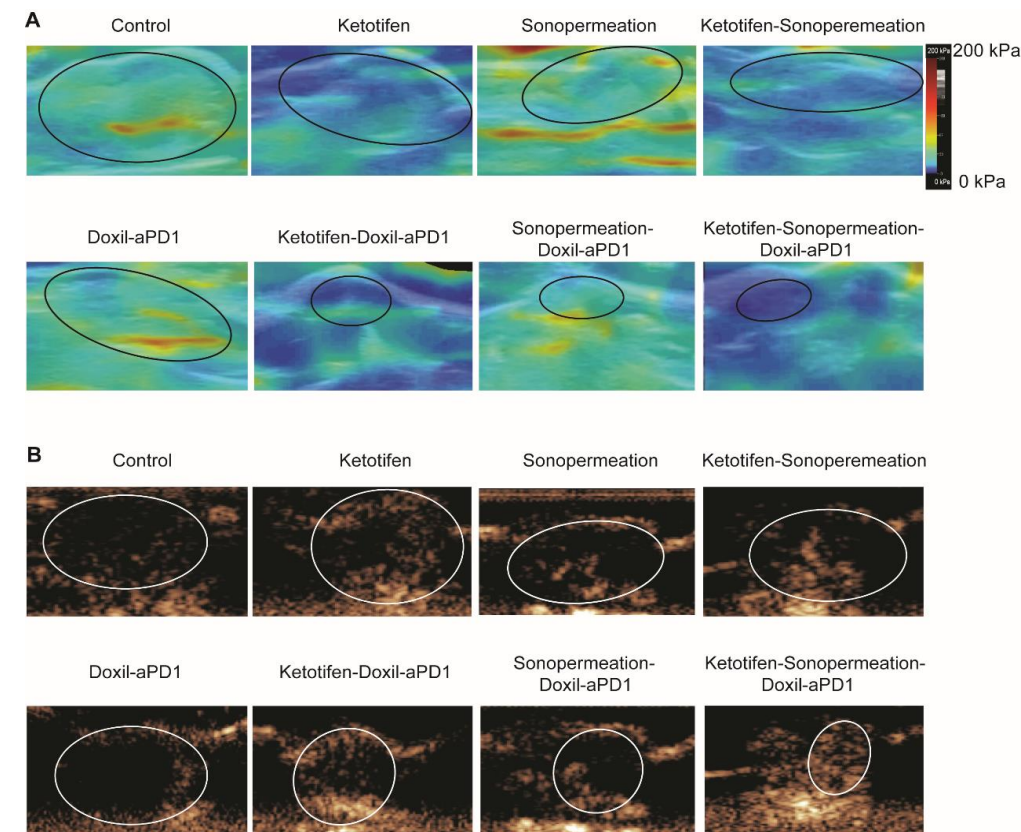
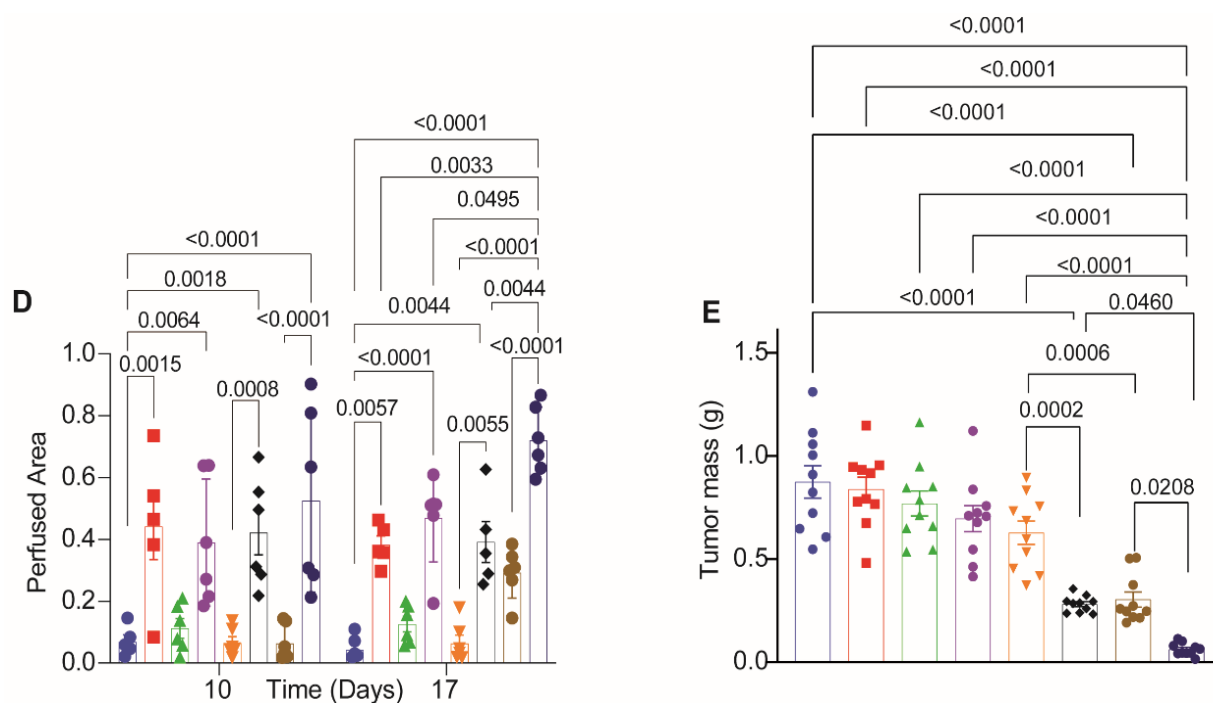


# Combined treatment improve the efficacy of nano-immunotherapy in fibrosarcomas



Mpekris F. et al, Neoplasia, 2024

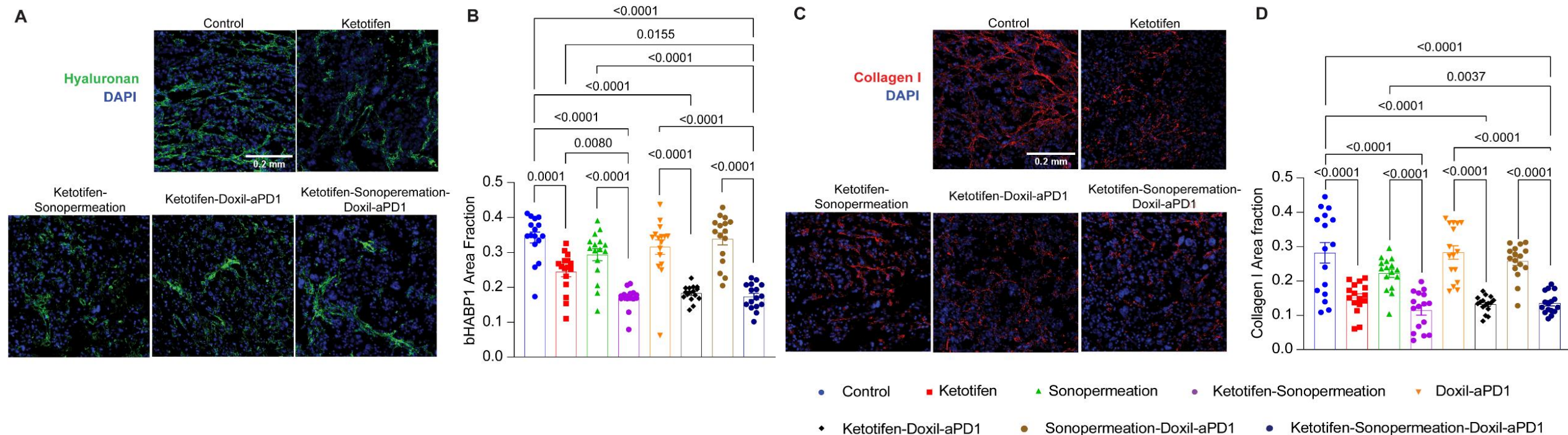
# Combined treatment improve the efficacy of nano-immunotherapy in fibrosarcomas



Mpekris F. et al, Neoplasia, 2024

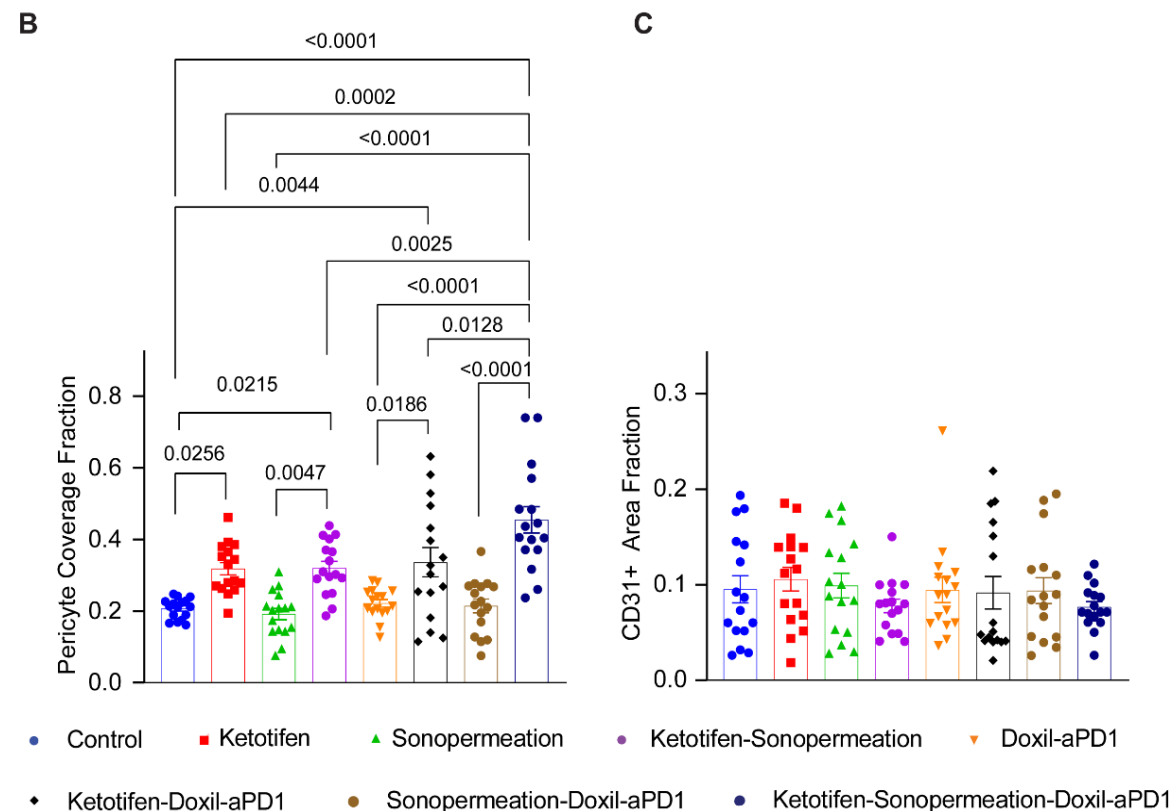
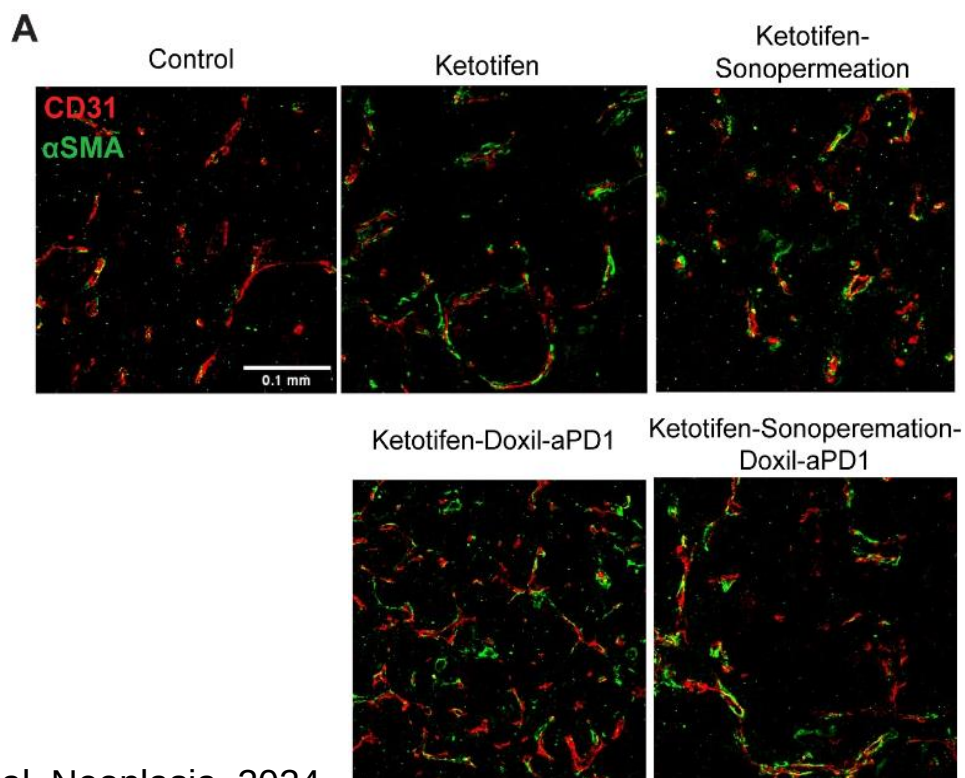


# Combination therapy decreased hyaluronan and collagen levels



Mpekris F. et al, Neoplasia, 2024

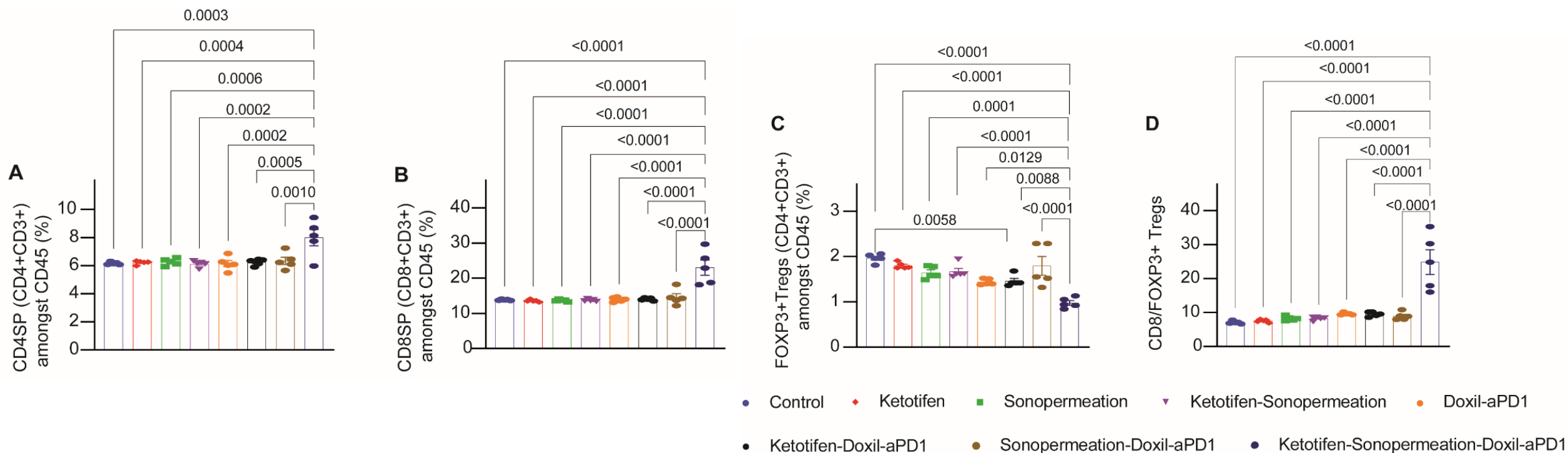
# Combination therapy normalized tumor blood vessels



Mpekris F. et al, Neoplasia, 2024

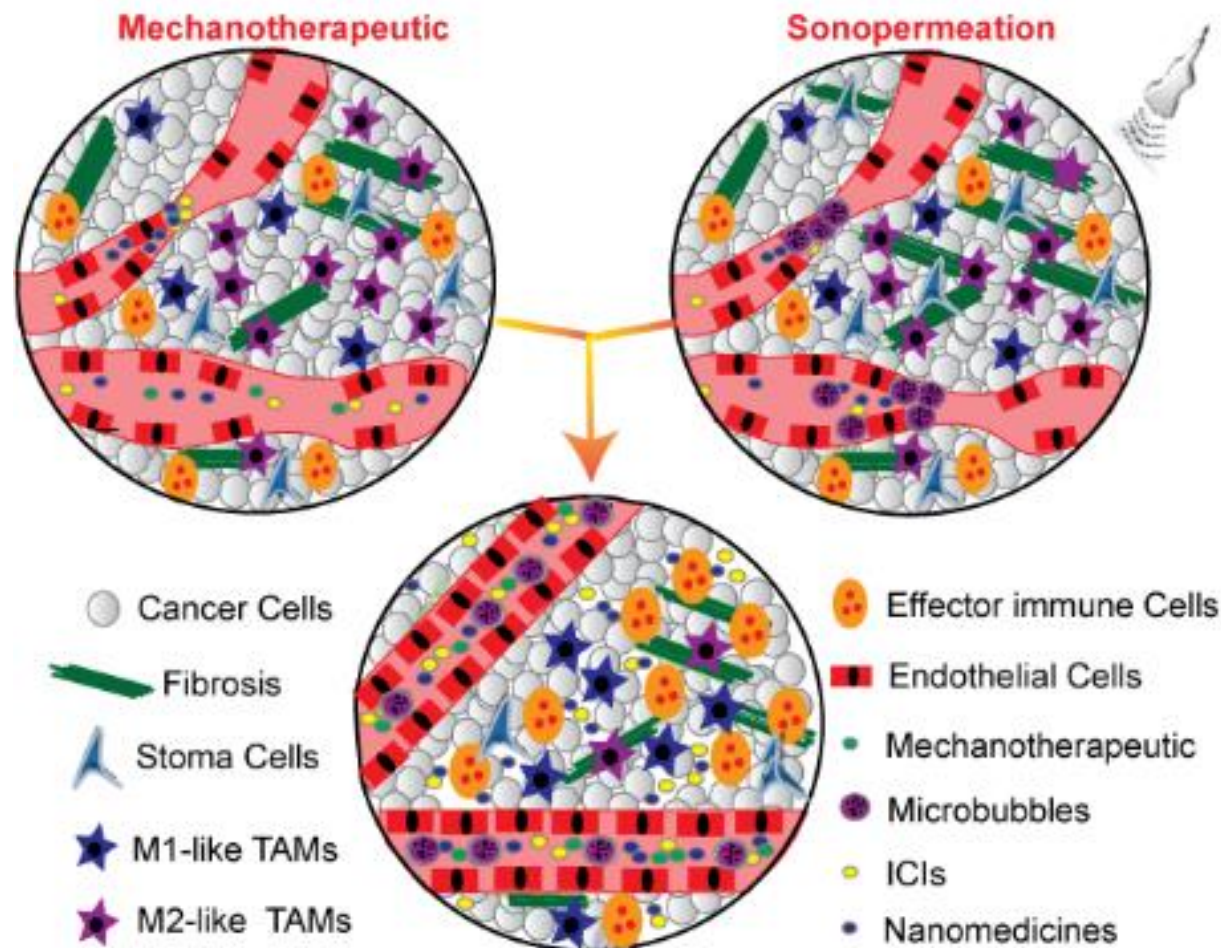


# Combination therapy enhanced immune cells infiltration



Mpekris F. et al, Neoplasia, 2024

# Conclusions



Mpekris F. et al, Neoplasia, 2024



# Acknowledgements

## ***Cancer Biophysics Laboratory & Tumor Mechanopathophysiology Lab***

- Prof. Triantafyllos Stylianopoulos
- Dr. Constantina Neophytou
- Dr. Chrysovalantis Voutouri
- Dr. Myrofora Panagi
- Dr. Antonia Charalambous
- Ms. Christina Michael
- Ms. Antonia Papoui



European Research Council  
Established by the European Commission

ERC Starting Grant  
“MMSCancer”

