

High-throughput 3D light-sheet imaging of mouse hindlimb enable skeletal muscle morphometrics in muscle wasting models

Authors

Max Hahn¹, Alex B. Addinsall¹, Anitta K. Sárvári¹, Kasper Andersen¹, Malte Hasle Nielsen¹, Estrid T. Pedersen¹, Marco Tozzi¹, Henrik B. Hansen¹, Nicolas O. Eskesen¹ and Urmas Roostalu¹

¹Gubra, Hørsholm Kongevej 11B, Hørsholm, Denmark



Corresponding author:

Max Hahn
mah@gubra.dk

Background & Aim

Conventional methods for assessing skeletal muscle remodelling, including lean mass, muscle weight, and histology, lack the spatial resolution and sensitivity to capture three-dimensional muscle architecture. Here, we developed a scalable, non-destructive, AI-enabled light-sheet fluorescence microscopy (LSFM) platform for holistic 3D analysis of intact mouse hindlimbs. We aimed to validate the platform across pharmacological models by quantifying individual muscle volume and key structural features with anatomical precision.

Methods

Model: 48 Male C57BL/6J mice were randomized by body weight (BW) and lean mass. Mice received Vehicle (PBS) or dexamethasone (1.0 mg/kg, SC) daily for three weeks to induce muscle atrophy.

Therapy: Bimagrumab, Apitegromab or IgG-control (20 mg/kg, SC or IP) were administered weekly, starting on the first day of dexamethasone treatment.

Assessments:

- + BW were recorded daily, while EchoMRI assessed body composition weekly.
- + Individual muscles were weighed and histopathology assessed.
- + Whole hindlimbs were collected & processed for autofluorescence based 3D light sheet fluorescence microscopy (LSFM) and high-resolution volume acquisition.
- + Whole lower hindlimb immunohistochemistry for visualization of muscles health (fibrosis, innervation and vasculature).

Method:

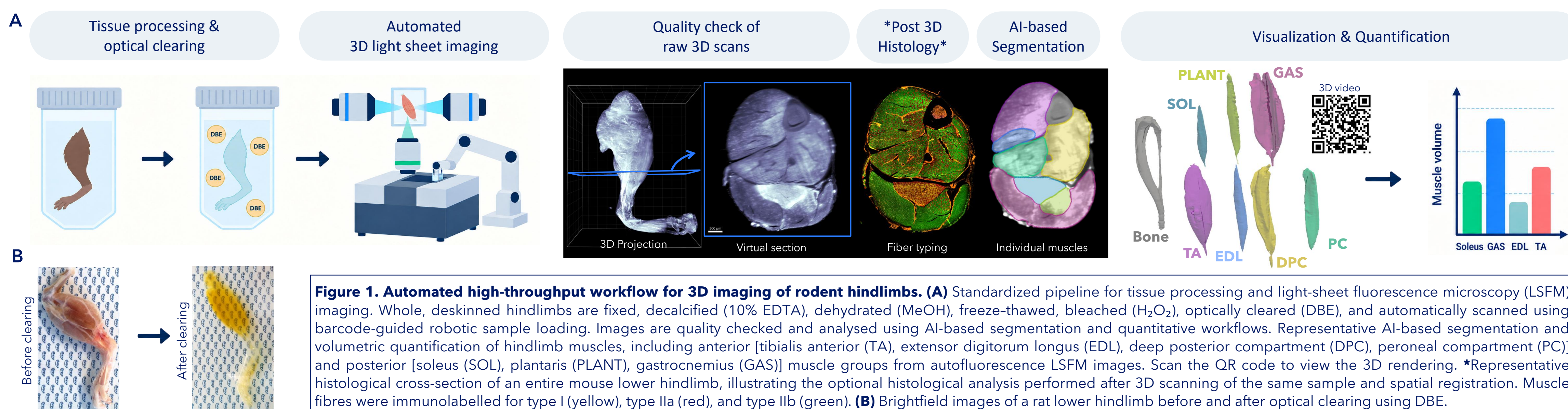


Conclusion

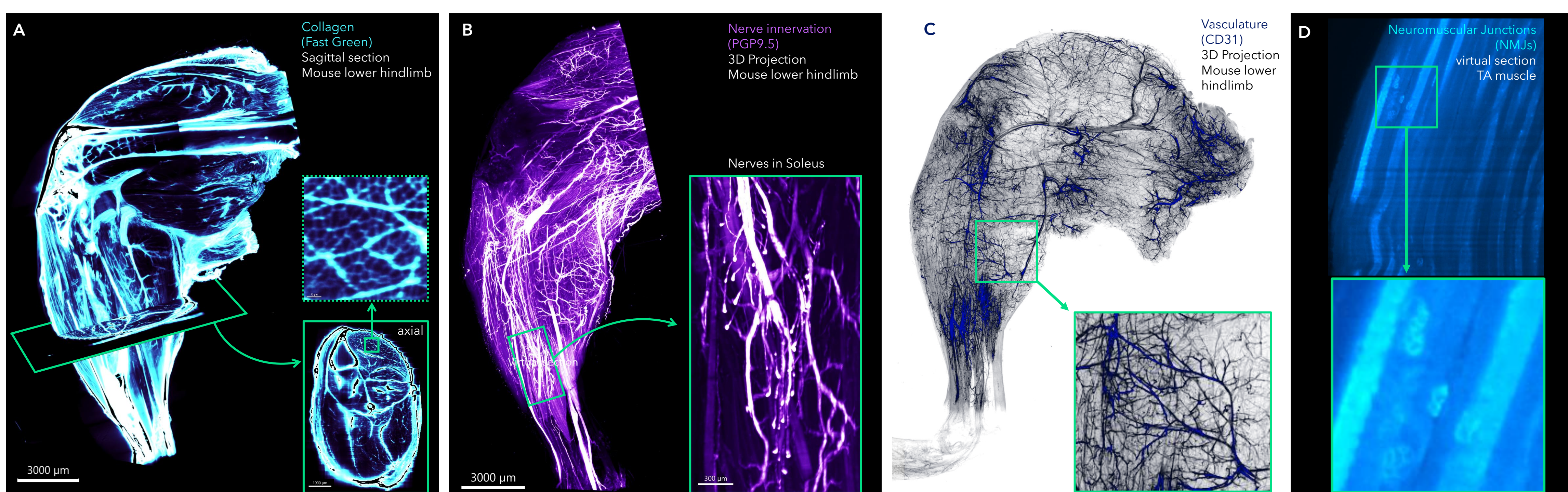
- + Three-week dexamethasone treatment provides robust muscle wasting to test novel muscle-sparing or -promoting pharmacotherapies.
- + Bimagrumab and Apitegromab attenuate dexamethasone-induced changes in body composition, muscle mass, volume, and fiber size.
- + Our 3D muscle volume endpoint provides spatial resolution beyond lean mass scans, bridging MRI and histological assessment.

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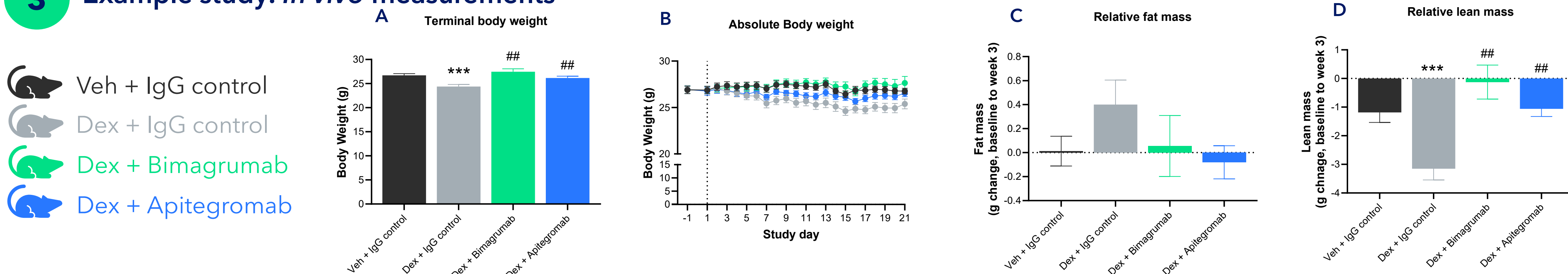
1 3D skeletal muscle imaging pipeline: High-throughput, automated & non-destructive



2 Potential endpoints: 3D muscle imaging to visualize muscle health



3 Example study: In vivo measurements



4 Example study: Comparison of muscle weight, CSA and 3D muscle volume

