



Early-Onset Metformin Regimen Inhibits Radiation-Induced Fibrosis In Mice Model

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INTRODUCTION

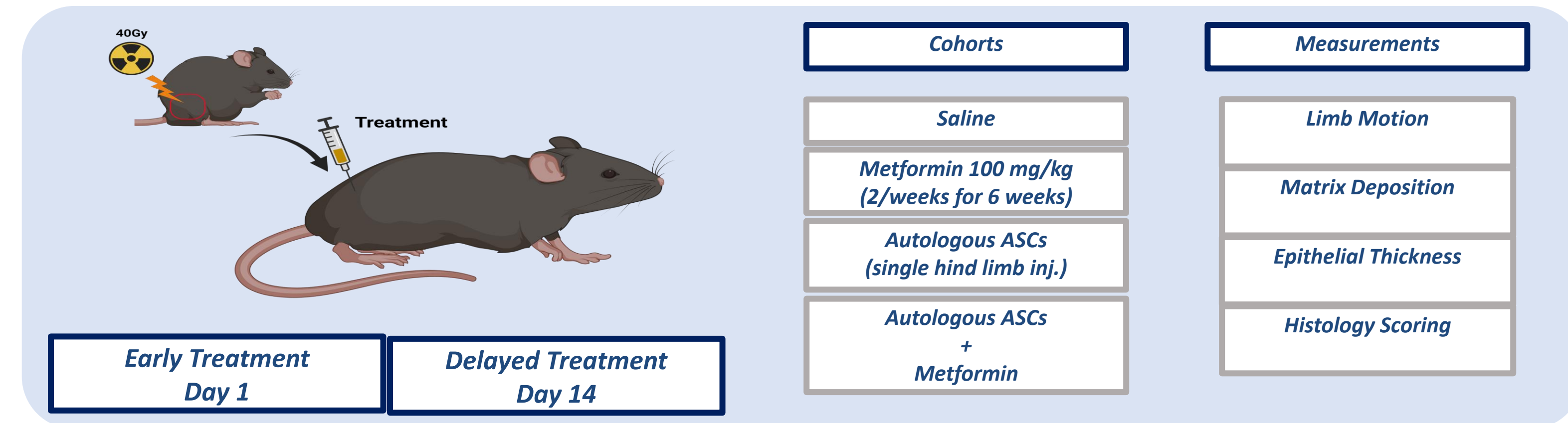
Radiotherapy is essential for cancer treatment, but it can cause radiation-induced fibrosis. Current treatments have achieved limited success.

Our previous research showed promising results with autologous cells and tissue engineered products. But they are difficult to use in a clinical setting.

AIM: To examine metformin treatments in both early and delayed settings to mitigate radiation-induced fibrosis.

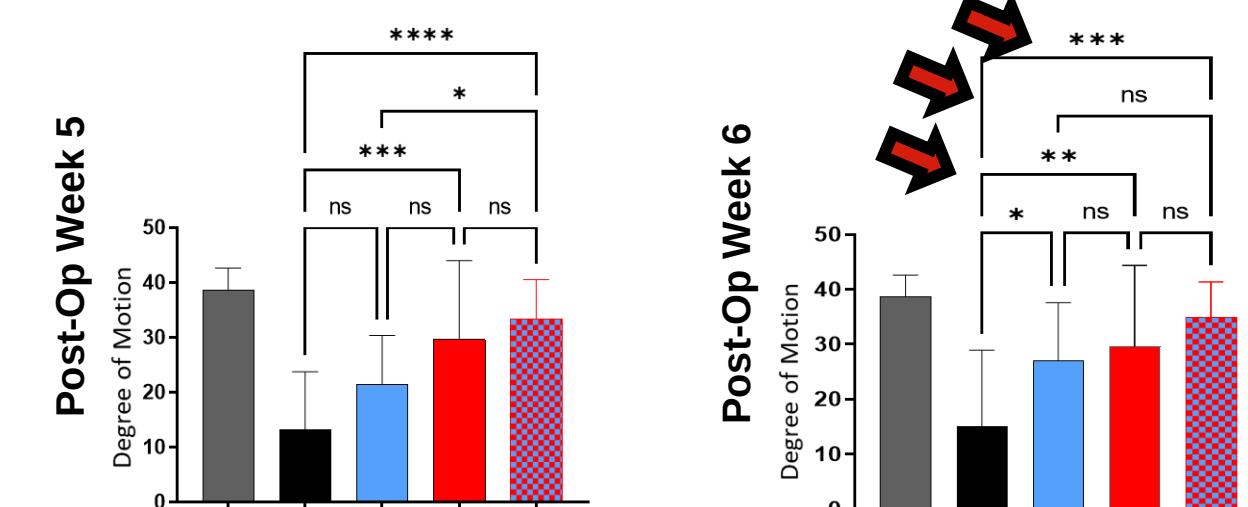
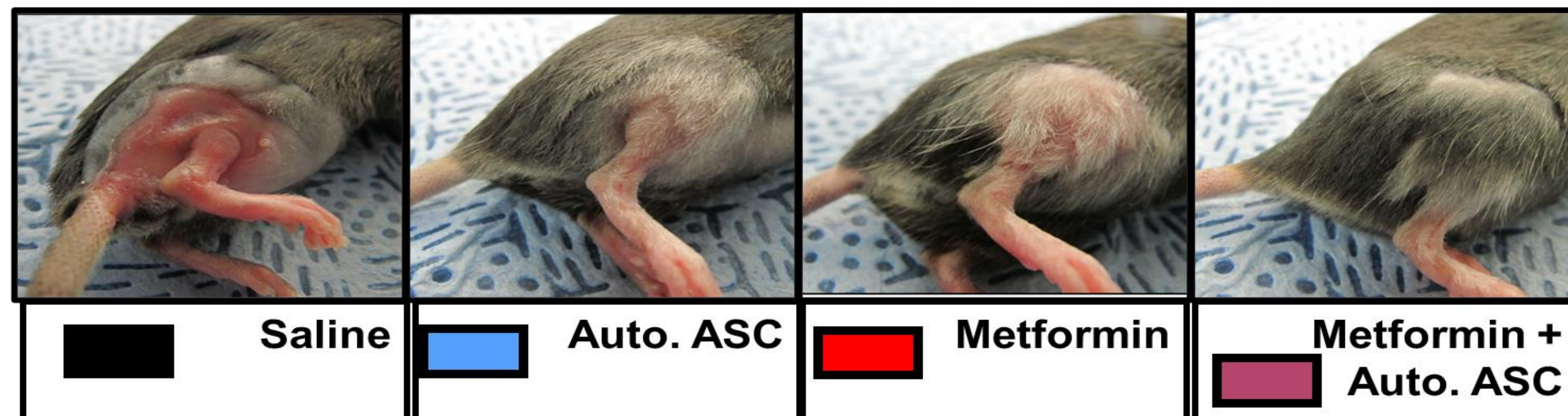
METHODS

Using a mouse model of radiation-induced fibrosis, we created eight different cohorts to test the efficacy of early and delayed treatment.



We irradiated the hind limb on day 0 and created cohorts for early and delayed treatments. These included IP metformin injection, single local autologous stem cell injections, and metformin regimen with or without stem cell injection starting on days 1 and 14.

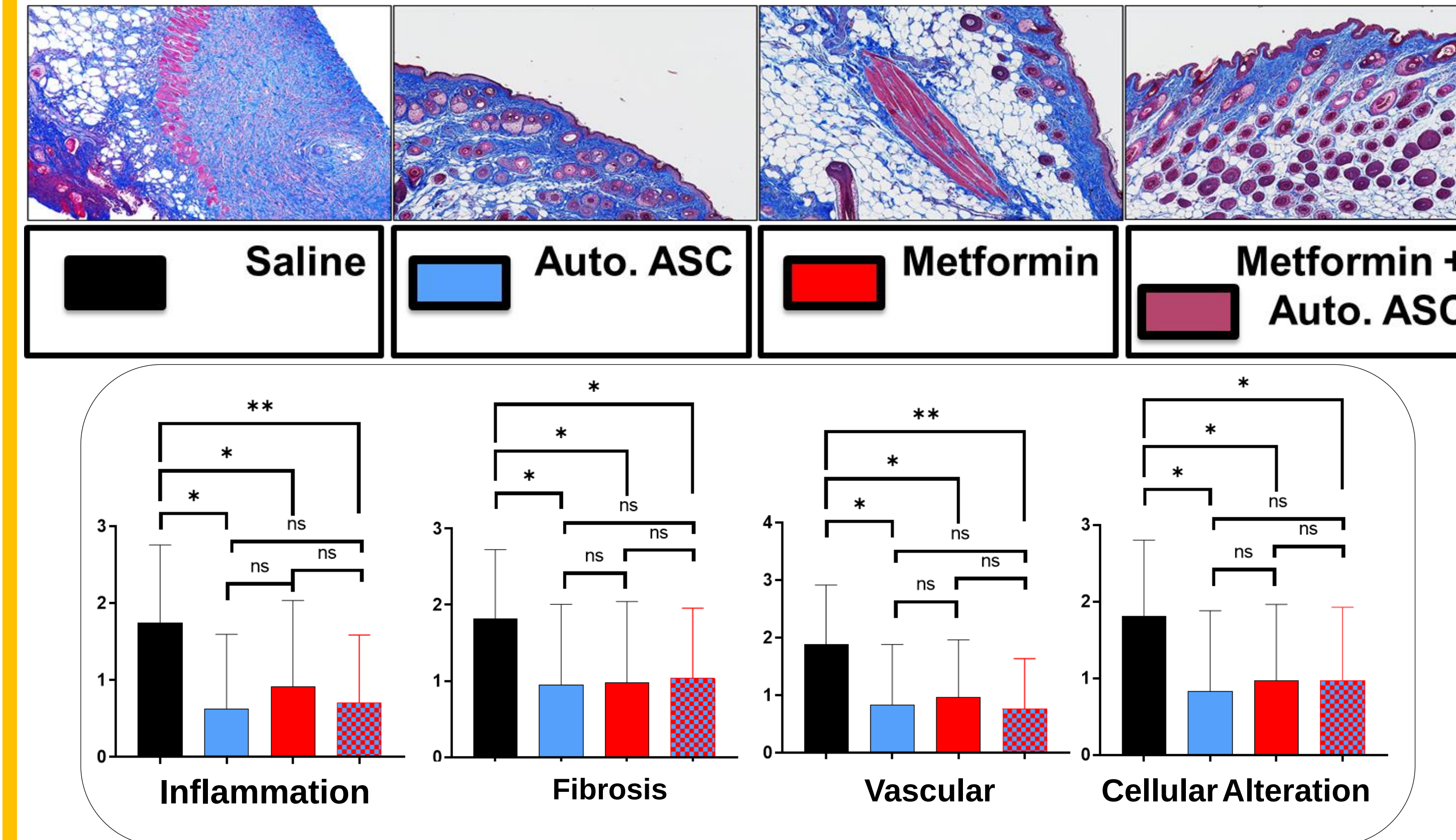
RESULTS – Early Treatment



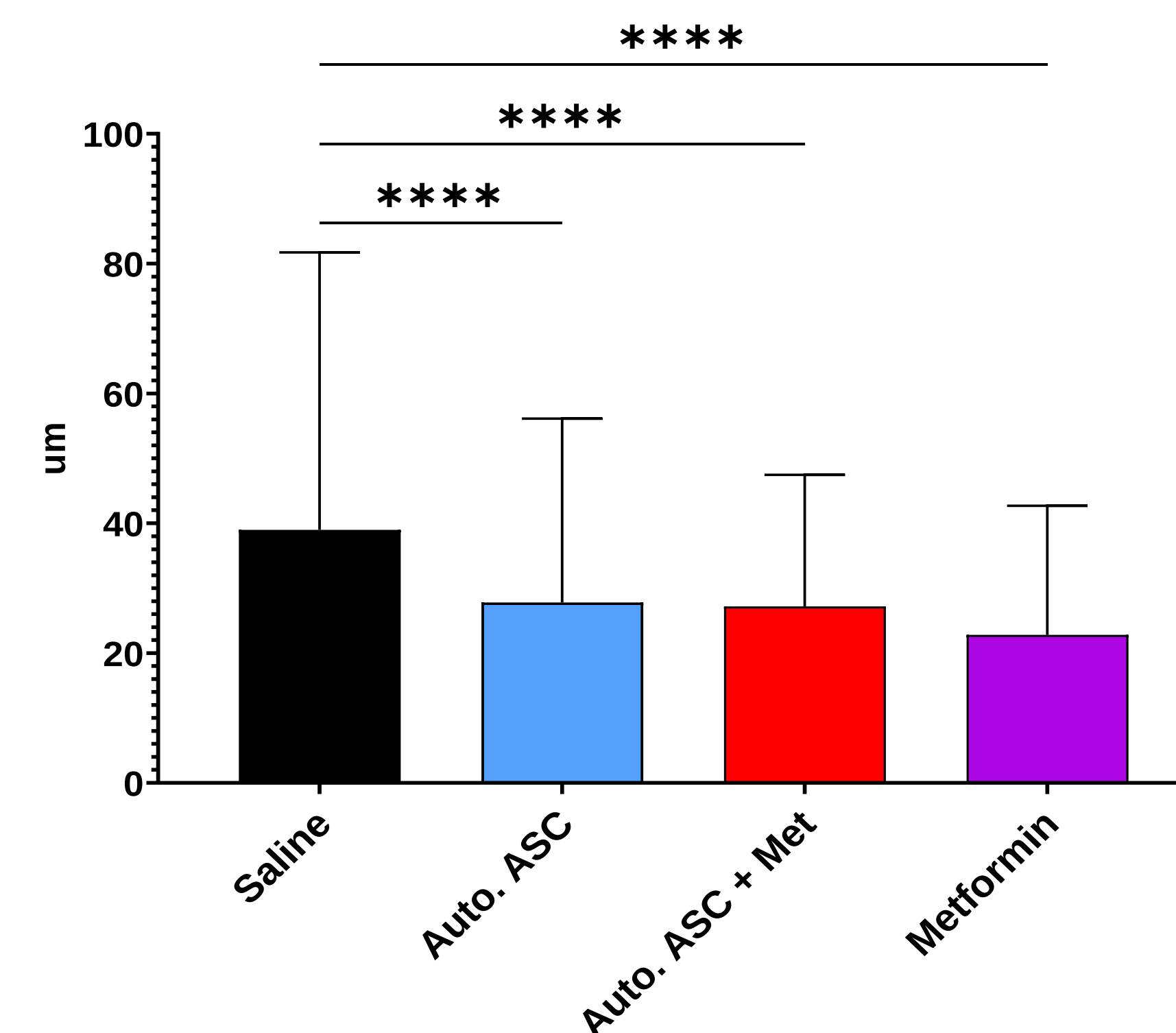
Autologous ASC and metformin performed comparably.

*= p<0.05 **=p<0.01 ***=p<0.001, ****=p<0.0001

RESULTS – Early Treatment

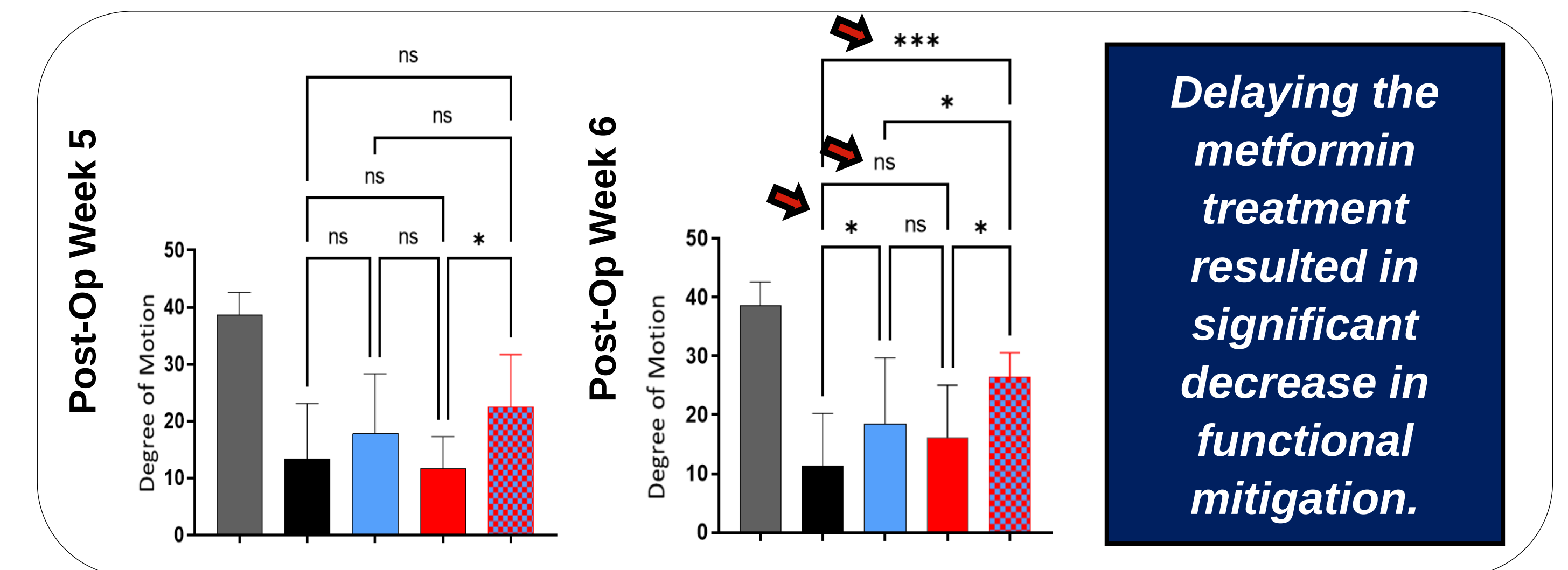
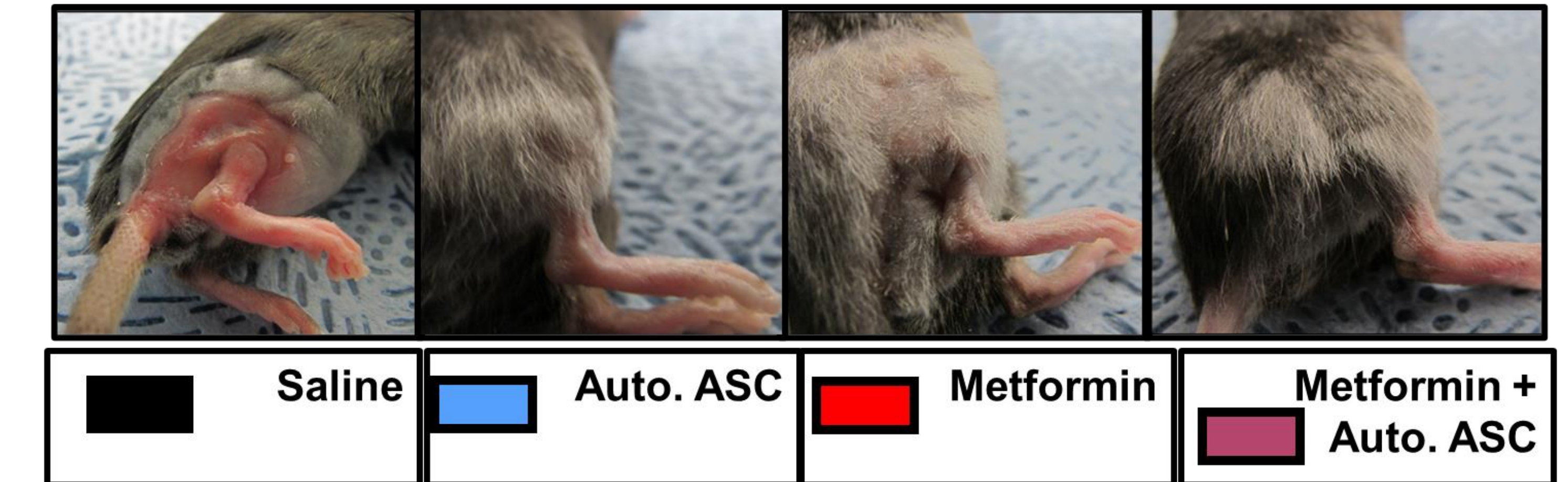


Early treatment with metformin prevented excessive matrix deposition and loss of skin appendages achieving fibrosis scores and functionality comparable to ASC injections.



Early treatment led to significant improvement in epithelial thickness in both metformin and cell-based treatments.

RESULTS – Delayed Treatment



Delaying the metformin treatment resulted in significant decrease in functional mitigation.

When metformin treatment was delayed to 14 days, it resulted in better gross examination outcomes but comparable functional restrictions to the control group.

In contrast, cell therapies remained significantly better than the control group even when injected after 14 days.

CONCLUSION

Systemic administration of metformin at a dose of 100mg/kg twice per week prevented fibrotic development in mice model, as demonstrated by the cohort that received the regimen starting on post-irradiation day 1.

Nevertheless, the preventive effect of metformin was not observed when the treatment was delayed until day 14, suggesting that metformin may be more useful as a prophylactic agent rather than a curative intervention for established cases of fibrosis.

Metformin has shown comparable success to stem cell therapies as a prophylactic agent.