

The Effects of Cisplatin on Gastrostomy Site Healing

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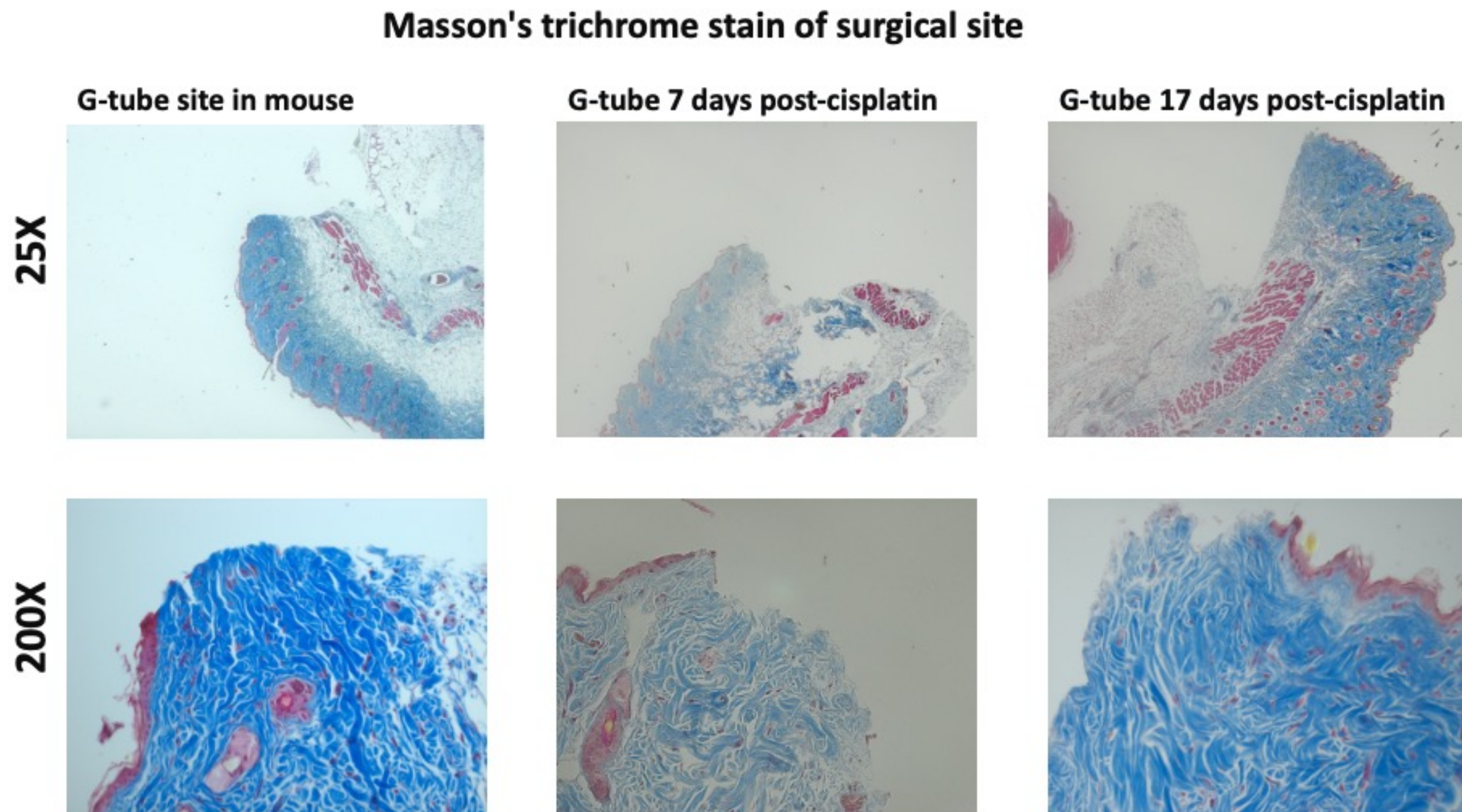
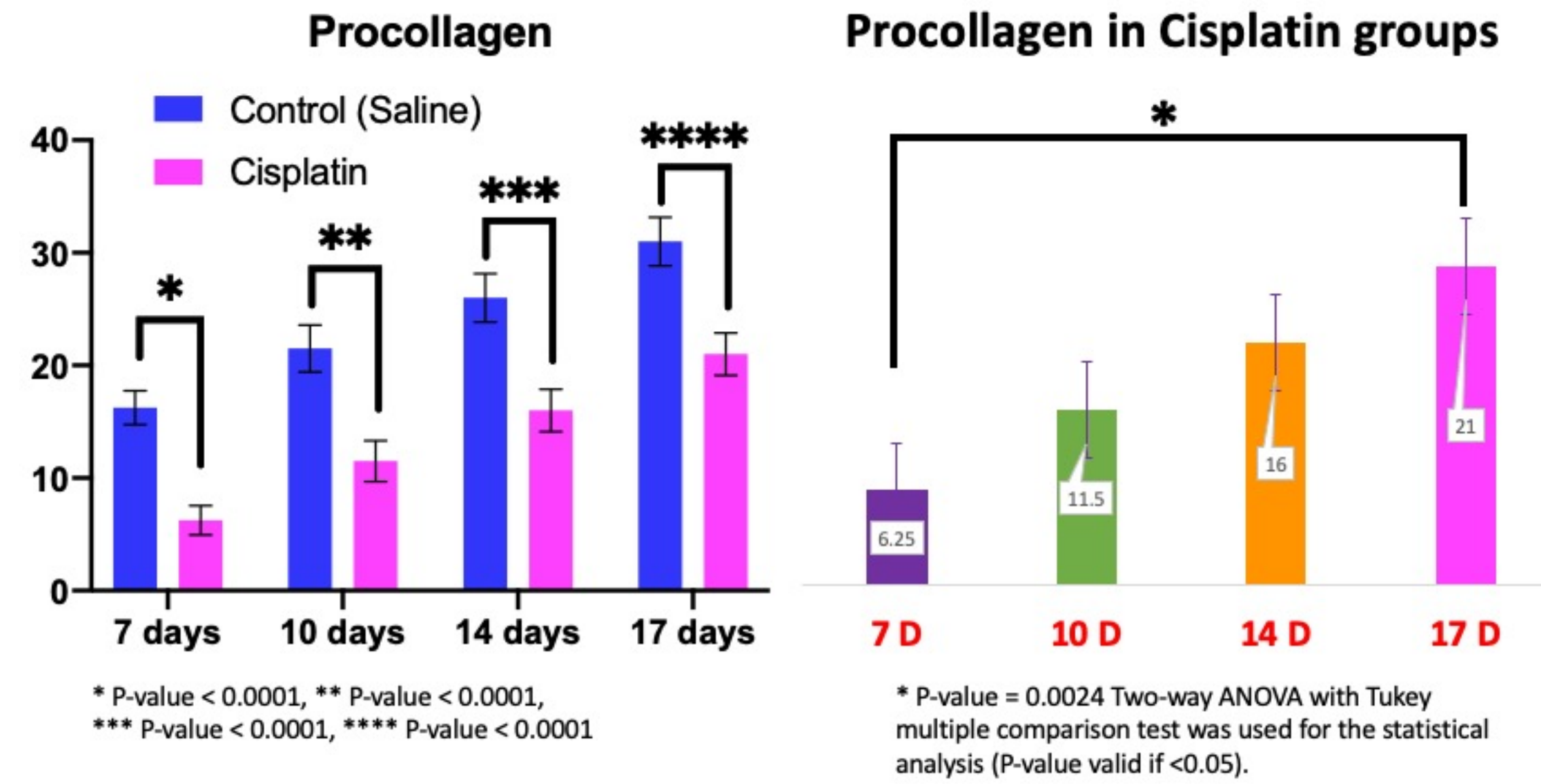
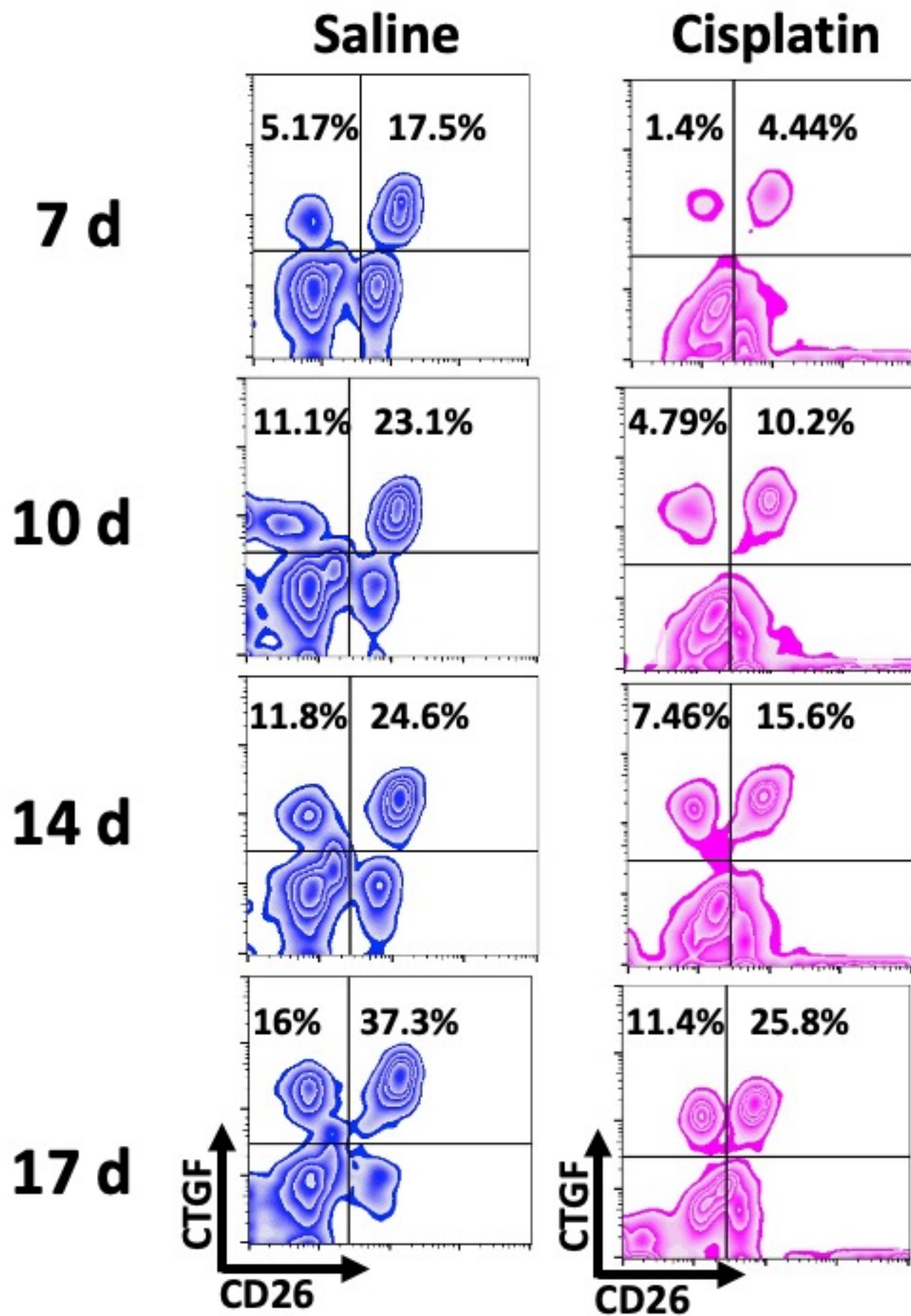
INTRODUCTION

Patients with head and neck cancer face unique challenges to meeting nutritional needs while undergoing treatment. Radiation therapy results in mucositis and odynophagia, particularly in combination with concurrent chemotherapy. However, minimizing gastrostomy tube (G-tube) dependence is known to be beneficial for long term swallowing outcomes, therefore pre-treatment placement is performed judiciously. Some patients, initially presumed capable of po intake, unexpectedly need supplementation and a G-tube must be placed after initiation of treatment. Cisplatin is known to affect tissue healing, however the effect on the site of gastrostomy tube placement has not been studied. We hypothesize that cisplatin impairs collagen formation with gradual reduction in toxicity over time. We examined healing gastrostomy sites in mice while varying the time from cisplatin dosing to gastrostomy placement.

METHODS

Sixteen mice were administered 1 mg/kg cisplatin by intraperitoneal route. The mice were divided into four groups with four mice in each, undergoing a novel mouse gastrostomy technique on post-chemotherapy days 7, 10, 14, and 17. Mice were sacrificed 10 days after placement of the gastrostomy tube and the tissue surrounding the site was harvested. Formalin-fixed paraffin-embedded gastrostomy site tissues were sectioned and stained with Masson’s trichrome. The collagen was compared. Samples from the gastrostomy sites were also prepared for flow cytometry analysis comparing levels of connective tissue growth factor (CTGF), procollagen type 1, and CD26. Sixteen control mice with four mice in each group underwent saline infusion rather than cisplatin infusion, followed by gastrostomy tube placement at the same time points for comparison. There was also a control mouse that only underwent gastrostomy tube placement and was sacrificed 10 days after placement.

RESULTS



Masson’s trichrome staining shows scant collagen formation in surgical site tissue from mice that were 7 days post-chemotherapy. In contrast, the surgical site tissue from mice that were 17 days post-chemotherapy had collagen similar to a mouse that had gastrostomy placement alone. Levels of procollagen type 1 were significantly higher in the control group compared to the treatment group with $p < 0.0001$ for each time point. When comparing the treatment groups, there was a statistically significant difference in procollagen type 1 between the 7 days post-chemotherapy group and the 17 days post-chemotherapy group ($p = 0.0024$). The percentage of cells with procollagen in the 7 days post-saline control group were similar to the percentage in the 14 days post-cisplatin treatment group. The same was true of the levels of cells positive for both CTGF and CD26; levels at 14 days post-cisplatin were comparable to levels at 7 days post-saline.

CONCLUSIONS

As expected, healing was impacted by cisplatin with significantly less CTGF, CD26, and procollagen at each time point when compared to saline. The results show that the levels 14 days after a cisplatin treatment approximate the levels 7 days after saline. Additionally, procollagen is significantly higher in the surgical site when performed 17 days after cisplatin when compared to 7 days after cisplatin. This was confirmed qualitatively with the Masson’s trichrome stain.

CLINICAL IMPLICATIONS

Other things being equal, the results suggest that it is safe to proceed with gastrostomy tube placement 14-17 days after cisplatin because the CTGF, CD26, and procollagen levels in this timeframe approximate the levels 7 days after saline. Furthermore, the procollagen levels 17 days after cisplatin are much improved compared to levels 7 days after cisplatin. This new data can help guide providers and patients on the timing of post-cisplatin gastrostomy tube placement as they carefully weigh the risks and benefits of individual cases.

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