Radiographic Quantification of Tracheal Autografts

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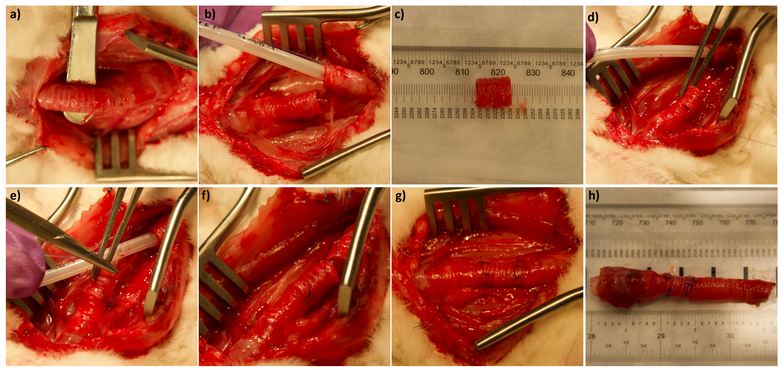
Abstract

Background:
Tracheal defects ultimately require tissue replacement for adequate reconstruction. We previously demonstrated the use of partially decellularized tracheal grafts to support regeneration of tracheal neotissue, however there is increased graft calcification in vivo. To distinguish graft versus surgical causes of cartilage calcification, we used a rabbit model of tracheal autograft and performed surveillance imaging of the graft in vivo. We hypothesize that tracheal autografts maintain patency and that grafts would demonstrate higher calcification at 3 and 6 months compared to native trachea.
Methods:
Four male New Zealand White Rabbits underwent tracheal autograft. Briefly, a ~1 cm segment of trachea was resected and reimplanted. Three-dimensional (3D) fluoroscopy was performed at day-0, at 3 and 6 months. Three-dimensional reconstructions of the graft were created to calculate the average luminal area and quantify the Hounsfield units (HU) normalized by host. At endpoint (6 months), grafts were explanted and ex vivo imaging with HU quantification was performed using microCT.
Results:
All animals survived to endpoint without signs of respiratory distress. Grafts remained patent throughout the time points and remained equivalent to host airway dimensions ($p>0.05$). There was an increase in autograft HU seen with microCT at the 6 month timepoint ($p<0.05$), indicating graft calcification. This increase in calcification was not observed in native trachea or adjacent host trachea.
Conclusions:
Surgical management of the trachea results in an increase in graft calcification, which appears to increase over time. Orthotopic tracheal replacement does not result in changes in graft area after surgery. This suggests that calcification is part of the wound healing and remodeling of tracheal implantation. The impact of calcification on graft mechanics and graft viability remains unclear.

Background

- Long segment tracheal defects ultimately require tissue replacement for adequate reconstruction
- We previously demonstrated the use of partially decellularized tracheal grafts to support regeneration of tracheal neotissue, but there is increased graft calcification in vivo, which has been largely attributed to chondrocyte apoptosis
- It is possible that the observed calcification is not a graft-dependent phenomenon and may be related to postoperative healing from orthotopic tracheal replacement
- Tracheal autograft is the gold standard surgical control of tracheal grafts, it is necessary to quantify the impact of tracheal resection and anastomosis and the healing process on graft patency and dimensions to establish a baseline comparison.
- Objective: Radiographically quantify changes in graft dimensions over time and distinguish graft versus surgical causes of cartilage calcification to establish anticipated imaging findings in control surgeries

Figure 1. Orthotopic tracheal replacement with autograft



a) Exposure of rabbit trachea **b)** Inferior trachea cut and insertion of endotracheal tube through incision **c)** Excised rabbit trachea autograft **d)** Superior anastamosis of autograft **e&f)** Inferior anastomosis of autograft **g)** Completed tracheal autograft resection and reanastamosis **h)** Explanted rabbit trachea with autograft

Hypotheses

- We predicted that tracheal autografts would:
  1) maintain similar dimensions at 3 and 6 months to day 0
  2) demonstrate higher calcification at 3 and 6 months on microCT compared to day 0 and compared to native trachea

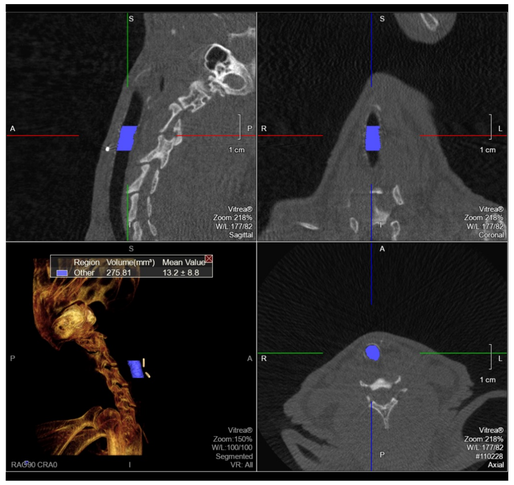
Methods and Materials

- Four male New Zealand White Rabbits underwent tracheal autograft surgery.
- A ~1 cm segment of trachea was resected and reimplanted, similar to previously described mouse autograft **(Figure 1)**.
- Three-dimensional (3D) fluoroscopy was performed at day-0, at 3 and 6 months.
- Three-dimensional reconstructions of the graft were created to calculate the average luminal area and quantify the Hounsfield units (HU) normalized by host (**Figure 2**).
- At endpoint (6 months), grafts were explanted and ex vivo imaging with HU quantification was performed using microCT (**Figure 3a, b**)

Results

- All animals survived to 6 month endpoint without signs of respiratory distress
- There was an increase in autograft HU seen with microCT at the 6 month timepoint ($p<0.05$), indicating graft calcification (**Figure 3c)**
- This increase in calcification was not observed in native trachea or adjacent host trachea (**Figure 3d)**
- Grafts remained patent throughout all time points and remained equivalent to host airway dimensions ($p>0.05$) (**Figure 3e**)

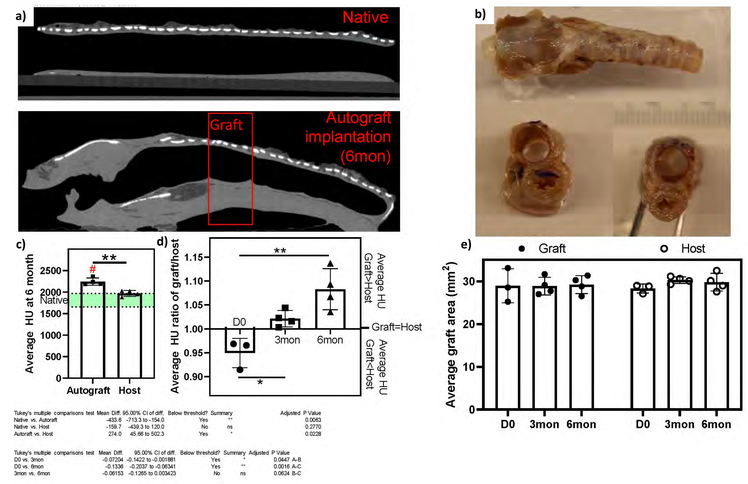
Figure 2. Radiographic measurements of tracheal autograft dimensions



Discussion

- Orthotopic tracheal replacement does not result in changes in graft area due to surgery.
- However, surgery appears to increase calcification of tracheal autografts compared to host and native trachea and these changes increase over time.
- This suggests that calcification is part of the healing process of tracheal grafts and serves as a baseline quantification for use of orthotopic rabbit models as surgical controls on radiographic studies of tracheal grafts in the future.
- Further studies are needed to explore histologic changes associated with calcification and explore the role of tracheal calcification in wound healing and tracheal replacement.
- The impact of calcification on graft mechanics and viability remains unclear.

Figure 3. Results of radiographic quantification of tracheal autografts



Conclusions

We established that orthotopic tracheal replacement in a rabbit model does not result in changes in graft area but does appear to increase calcification of the autograft when compared to host or native trachea. These results suggest a baseline of calcification that could be used to normalize surgical controls when comparing to tracheal grafts. Further studies are needed to understand the mechanisms and role of calcification in tracheal grafts.

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