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In vivo characterization of metabolic activity and oxidative stress in grafted human ovarian tissue using microdialysis

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Context: As ovarian tissue (OT) transplantation for fertility restoration purposes is performed without vascular anastomosis, graft viability depends on progressive revascularization. Human OT revascularization is initiated after 3-5 days and stable partial pressure of oxygen (pO2) levels are reached after 10 days, as shown in Van Eyck et al's study. However, the role of oxidative stress and metabolic changes occurring in grafted OT are still unknown.

Objective: To characterize oxidative stress and metabolic activity in grafted human OT.

Methods: Xenotransplantation of human OT in murine back muscle; daily measurements using microdialysis for lactate, glucose and reactive oxygen species (ROS) levels (using Amplex UltraRed); histological and immunofluorescence OT analysis (human: vWF; murine: CD31; polyclonal ?SMA) on days 10 and 21 post-transplantation.

Patients: OT from 5 patients (mean age 29.4 ± 3.2).

Interventions: Ten nude mice were grafted with OT, into which a microdialysis probe was inserted.

Main outcome measures: Daily (ROS), lactate and glucose levels; follicle loss after 10 and 21 days; revascularization from host and graft components and vessel stabilization.

Results: Lactate levels were significantly higher than glucose levels until day 10, after which time the lactate:glucose ratio stabilized at around 1:1. Regarding ROS generation, there were two peaks on post-grafting days 10 and 17. Total vascularization increased significantly up to day 10 and stabilized up to day 21. However, murine vessel area and stabilization significantly increased up to day 21. Major follicle loss occurred in the first 10 days post-transplantation.

Conclusion: Grafted OT goes through a progressive shift to aerobic metabolism, completed only after 18 days. ROS generation starts after 10 days, when pO2 levels are stable, and continues until vessel stabilization. Major follicle loss occurs earlier than major ROS generation.

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