External Mechanical Forces Alter Development Of Mammary Gland

During puberty, the mammary gland forms an extensive network of epithelial ducts that are vital for milk secretion. Mechanical forces are believed to play a key role in the development of the ductal network; however, this process is not fully understood. We aim to study if mechanical forces impact branching development. This research yields information on how exogenous mechanical forces regulate mammary gland development. By improving our understanding of mammary gland development, we can gain insight into how the gland dysfunctions in diseases such as breast cancer. At five weeks, the skin surrounding the left abdominal number four mammary gland nipple of female mice were adhered together with surgical glue to create a tensional force (TEN). At seven weeks of age, the abdominal glands were removed and whole mounts prepared. Using image analysis, we compared the ductal morphology of the TEN glands to the untreated-control (CTL) mice. We found that the TEN glands grew significantly longer than the CTL glands, despite no significant difference in size. Further analysis found significance in the branching angle between TEN and CTL. In-silico simulations of branching morphogenesis predict that branching angle alters the length of glands. These findings highlight the need to further understand how the mechanical environment impacts mammary gland development and long-term function.

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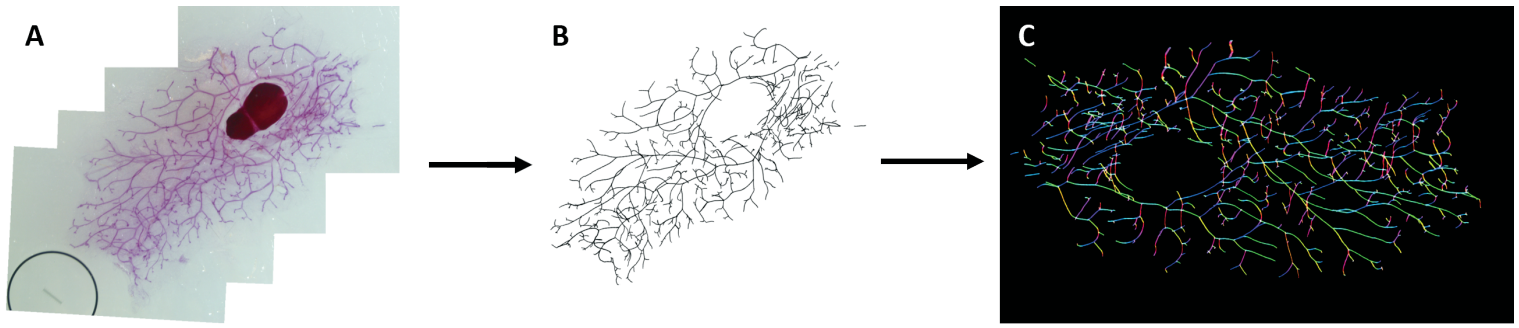
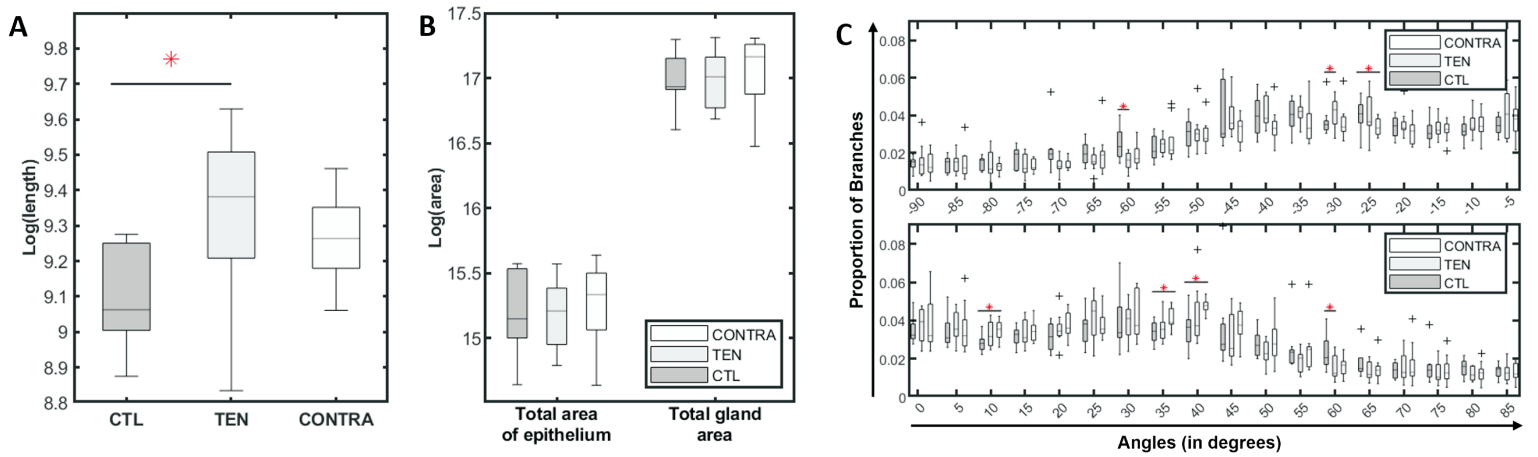
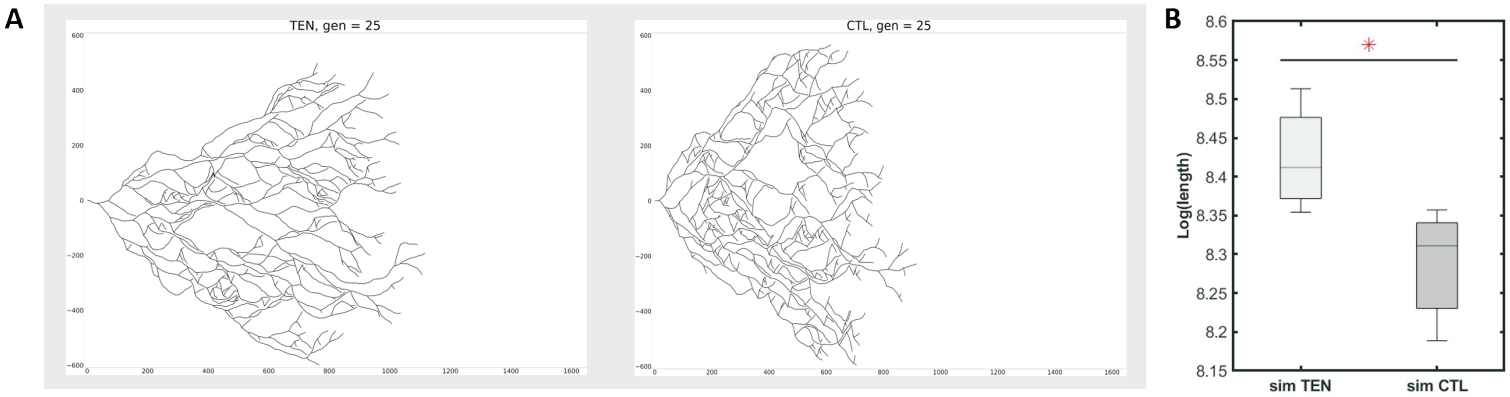


Digital image analysis: A) a microscopy image of the mammary gland, B) is an image of the branched network of the mammary gland epithelial tissue obtained using Photoshop and C) is a color map that depicts the orientation/angular position of the epithelial branches. This was obtained using OrientationJ software package.



Findings from the image analysis: A) The overall length of the branching network was significantly longer in TEN than CTL. B) No significant difference in the total area of the epithelium tissue and the total area of the mammary gland between TEN and CTL, despite the differences in overall length of the branched epithelium network. C) Box plot of the proportion of the epithelium branches in different angular positions show differences in branch orientations between TEN and CTL. In mice, there are five pairs of mammary glands. Here CONTRA denote the contralateral glands, that is the glands that were on the opposite side of the TEN glands.



In-silico branching and annihilating random walk model predicts that branching angle alters the overall length of the epithelium network: A) Simulations of TEN and CTL modeled with angle preference (30- and 60-degrees respectively) B) shows that the simulated TEN glands grew significantly longer than simulated CTL glands. gen denotes the number of generations of branching.