Impact of age and castration on canine prostate collagen organization

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Prostate-related urinary signs such as incomplete bladder emptying and straining are common in older intact male dogs and men. A longstanding paradigm is these symptoms derive from an aging-related increase in prostate volume but new evidence suggests additional mechanisms. For example, human prostatic collagen content was recently associated with tissue stiffness and urinary retention. The implications of which are huge for the veterinary community because treatment of fibrosis would not impact fertility like current alpha reductase inhibitors. The present study tested whether canine prostatic collagen increases with advancing age and whether castration reduces prostatic collagen content. We also used mice as a tractable model to test whether castration changes baseline urination and whether testosterone supplements reverse these changes. The canine study involved prostates obtained at necropsy divided into four groups: young (≤3 years) intact, young neutered, old (≥5 years) intact, and old neutered (n=9, 4, 4, and 14 respectively). Formalin fixed paraffin embedded prostate sections were stained with picrosirius red (PSR), imaged with florescent microscopy, and quantitatively analyzed for collagen fiber thickness, length, and density using novel computer software (CT FIRE, developed at LOCI- University of Wisconsin-Madison). The C57BL/6J mouse study design involved three groups: sham castrated, castrated + placebo implant, castrated + slow release testosterone implant (n=8). Urinary function was evaluated by anesthetized cystometry. Transverse canine prostate sections (figure) were characterized by four histologically distinct regions: urethral, periurethral, peripheral, and capsule. The prostatic urethra harbored a thick band of densely packed collagen. Collagen bundles radiated from the urethra and into the periurethral region where they branched before extending into the peripheral region. Collagen fibers in the peripheral region changed orientation before networking with the circumferential fibers of the capsule. Collagen fibers were denser in periurethral and peripheral regions of neutered male prostates compared to intact. Prostatic peripheral region collagen fibers were denser and the capsular collagen fibers thicker in old intact male prostates compared to compared to young intact males ($p = 0.0251$ and 0.0470, respectively). In mice, castration reduced void duration and time between voids, and testosterone supplementation returned void duration to that of intact but did not alter the reduced time between voids. Consistent with our hypothesis, this study revealed aging related increases in collagen density in intact males, and surprisingly castration was protective against these increases. Contrary to our hypothesis, castration resulted in increased glandular collagen density. These studies are the first to characterize regional collagen organization in the canine prostate and demonstrate the impact of castration on mouse voiding behavior. Supported in part by NIH U54 DK104310 & DK100227.

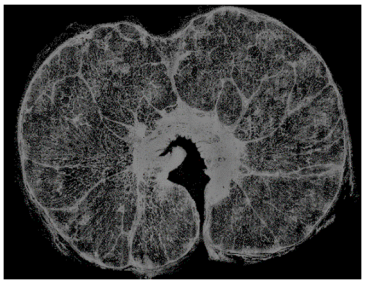

Figure. PSR stained prostate section imaged with fluorescent microscopy

Keywords: Benign prostatic hyperplasia, collagen, fibrosis, cystometry, prostate