Acta Biomaterialia xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

Acta Biomaterialia

journal homepage: www.elsevier.com/locate/actabiomat

Full length article

Characterization of facet joint cartilage properties in the human and interspecies comparisons

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ARTICLE INFO

Article history:
Received 24 December 2016
Received in revised form 21 February 2017
Accepted 10 March 2017
Available online xxxx

Keywords:
Biomechanics
Cartilage
Facet joint
Characterization
Properties

ABSTRACT

The facet joint, a synovial joint located on the posterior-lateral spine, is highly susceptible to degenerative changes and plays a significant role in back-related morbidities. Despite its significance, the facet is rarely studied and thus current treatment strategies are lacking. This study aimed to characterize, for the first time, the properties of human, pig, monkey, and rabbit lumbar facet cartilage providing much-needed design criteria for tissue engineering approaches. In this study, where possible, the facet's morphological, histological, mechanical, and biochemical properties were evaluated. Comparisons between the properties of the inferior and superior facet surfaces, as well as among spinal levels were performed within each species. In addition, interspecies comparisons of the properties were determined. The human facet joint was found to be degenerated; 100% of joint surfaces showed signs of pathology and approximately 71% of these were considered to be grade 4. Joint morphology varied among species, demonstrating that despite the mini-pig facet being closest to the human in terms of width and length, it was far more curved than the human or any of the other species. No notable differences were found in the mini-pig, monkey, and rabbit mechanical and biochemical properties, suggesting that these species, despite morphological differences, may serve as suitable animal models for studying structure-function relationships of the human facet joint. The characterization data reported in this study may increase our understanding of this ill-described joint as well as provide the foundation for the development of new treatments such as tissue engineering.

Statement of Significance

This work provides the first comprehensive description of the properties of lumbar facet joint cartilage. Importantly, this work establishes that histological, biochemical, and mechanical properties are comparable between bipedal and quadrupedal animals, helping to guide future selection of appropriate animal models. This work also suggests that the human facet joint is highly susceptible to pathology. The mechanical properties of facet cartilage, found to be inferior to those of other synovial joints, provide a greater understanding of the joint's structure-function relationships as well as the potential etiology of facet joint pathology. Lastly, this work will serve as the foundation for the development of much-needed facet joint treatments, especially those based on tissue engineering approaches.

1. Introduction

Zygapophyseal joints, frequently referred to as facet joints, are highly susceptible to the development of osteoarthritis (OA) [1]. These diarthrodial joints, located on the posterior-lateral spine, work with the intervertebral disc to transmit loads experienced by the spine while facilitating appropriate motion of the vertebrae (Fig. 1A). Depending on the nature of the spinal movement, the facet joints have been reported to carry up to 25% of the total spine compressive loads [2]. To compensate for a loss in structural integrity of a pathological intervertebral disc, the proportion of load borne by the facet joints can more than double [3]. Loading and abnormal loading of these joints can lead to the development of osteoarthritis.

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http://dx.doi.org/10.1016/j.actbio.2017.03.017
1742-7061/

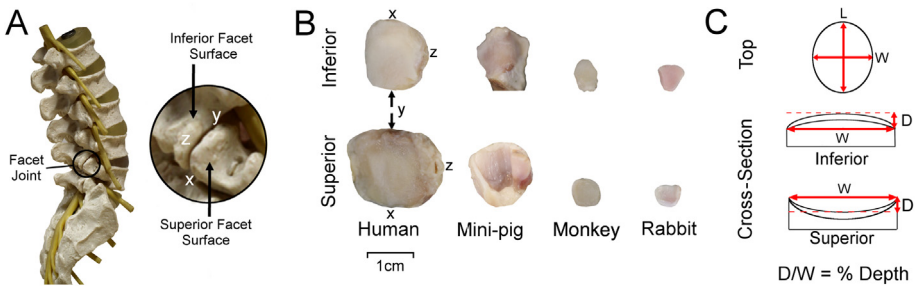

Fig. 1. Illustration of the facet joint anatomy and the gross morphological measurements of the facet joint surface. A) Location of the facet joint on the lumbar spine. Symbols x, y, and z denote the orientation of the facet joint in situ; this corresponds to the orientation of the joint once it is excised, as illustrated in (B). B) Example scaled images of the opposing inferior and superior facet joint surfaces excised between spinal levels L4 and L5 from the four species examined. C) Top view of the facet joint surface. The left to right and top to bottom arrows denote where the measurements of the width (W) and length (L) were taken for all joint surfaces, respectively. Measurements were taken at the widest and longest regions of the tissue. A cross-sectional view shows the arrows that correspond to the regions from which the W was measured for both the convex inferior and concave superior facet surfaces. A dashed line was constructed such that it ran parallel to the arrow denoting W and also through the lowest or highest point on the facet articular surface. The depth (D) is the perpendicular distance between the dashed line and the arrow. The percentage depth was calculated by normalizing D to W.

Facet OA is a universal finding in people over the age of 60 years old and affects approximately 60% of adults over the age of 30 years old [1]. Typical radiographic features of OA include joint space narrowing due to cartilage thinning, development of osteophytes and subchondral cysts, hypertrophy of the articular process, and subchondral bone sclerosis [4]. In a CT scan study of an older population (mean age 67 years old), the prevalence of moderate and severe lumbar facet joint OA was found to be approximately 86% and 50%, respectively [5]. Degeneration is most commonly found at the lower levels of the lumbar spine, i.e., L4-L5 and L5-S1; however, all spinal levels are susceptible [1,6–10].

Degeneration of the facet joint is known to play a significant role in back-related morbidities [11]. Advanced degeneration and concomitant hypertrophy of the facet joint can reduce the spinal canal size and impinge spinal neural elements, causing degenerative spinal stenosis. Spinal stenosis is the most frequently cited reason for lumbar spine surgery in the United States [12,13]. A similar trend is emerging in some European countries [14,15]. Facet joint pathology can also contribute to degenerative spondylolisthesis, where one vertebra translates with respect to the other. This condition occurs in 13.6% of the adult population [16] and contributes to both back pain and leg pain as the spinal cord or nerve roots are squeezed. In short, the facet joint is a significant source of back-related pathology.

In addition to its role in the aforementioned back-related morbidities, the facet joint is also thought to be the locus of low back pain on its own [17]. Similar to other synovial joints, the way by which pain manifests itself within the joint's structure is not well understood. However, the development of OA of this highly innervated joint has long been implicated as a potential cause of pain [5]. Despite the difficulties associated with diagnosis, the facet joints are estimated to be responsible for approximately 38% of chronic pain felt in the lower back [18]. Low back pain is currently the number one contributor to global disability [19] and is estimated to affect approximately 40% of people in their lifetime [20]. Although the prevalence of low back pain is highest between the ages of 40 and 80 years old, [20] young athletes have 3 to 5 times higher prevalence rates when compared to a general age-related population [21]. The debilitating nature of this disease has a huge impact on both the nation's health and health care system, at a total cost of approximately $200 billion per year [22,23]. Unfortunately, according to the latest global burden of disease report, the scale of the problem remains unchanged from 1990 to 2013. Furthermore, due to an aging population, low back pain has been predicted to increase in the coming years [19].

Due to the almost avascular and acellular nature of facet cartilage, it is unable to repair itself; pain alleviation is heavily dependent on medical treatment. Currently available, non-invasive treatment options only offer short-term relief. Treatments such as radiofrequency denervation, medial branch blocks, and intra-articular injections may reduce the symptoms temporarily but cannot provide a long term solution to the problem [24]. In cases of degenerative spinal stenosis and spondylolisthesis, surgical removal of the joints is often the only option. Removal of the facet joints can result in spinal instability necessitating fusion of the entire spinal segment. Like a domino effect, spinal fusion, in turn, is related to adjacent segment disease that encompasses a host of symptoms including hypertrophic facet arthritis in the neighboring vertebral segments [25]. Without suitable therapeutics, tissue engineering of the facet cartilage may serve as an attractive solution for long term motion-preserving pain management.

To date, there has only been one attempt to tissue engineer facet cartilage [26]. The paucity of work may primarily be due to the lack of published data detailing the characteristics of this tissue. In order to successfully engineer facet cartilage, it is critical that appropriate design criteria are established, which will ultimately provide the framework for the regeneration of a functional tissue replacement. Currently, there exist no experimental studies that characterize the biomechanical, biochemical, and histological properties of human cartilage, and only a few detailing the characteristics of animal facet cartilage [27,28]. With regard to the latter, the spines of quadrupeds receive different loading patterns when compared to bipeds, furthering the necessity for comparing the facet joints of humans and animals to develop suitable non-primate animal models.

Toward the long-term objective of tissue engineering facet cartilage replacements, the objectives of this study are 1) to characterize human lumbar facet cartilage and to compare it to mini-pig, monkey, and rabbit lumbar facet cartilage, using morphological, histological, biochemical, and biomechanical methods where appropriate, and 2) to compare properties according to anatomical location (i.e., spinal level and surface type) within and across species. The lumbar region of the spine was selected to study as it is associated with a high degree of pathology and is a popular target of therapeutics aimed to alleviate low back pain.

2. Materials and methods

2.1. Specimens

Human spines (n = 7, 4 female and 3 male) were obtained from Science Care and MedCure (see Table 1 for details). None of the human specimens were noted to have any known musculoskeletal pathology. Animal facet joints were harvested from the spines of

Please cite this article in press as: S.A. O'Leary et al., Characterization of facet joint cartilage properties in the human and interspecies comparisons, Acta Biomater. (2017), http://dx.doi.org/10.1016/j.actbio.2017.03.017