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The Natural History of Age-related Disc Degeneration

The Pathology and Sequelae of Tears

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Study Design. A quasi 3-dimensional pathologic survey of tears in the L4–L5 disc.

Objective. To seek accurate information on the pathogenesis and outcomes of tears to facilitate correlation with radiologic imaging and biomechanical testing; and to improve laboratory models for testing hypotheses of disc function and failure.

Summary of Background Data. Tears are evidence of structural failure involving the anulus. There are substantial differences in the structure and function of the anterior and posterior anulus and the nonlamellar "nucleus" is much smaller than generally conceptualized and modeled.

Method. Microscopy of sections prepared from 5-mm-thick parallel sagittal slices of 70 L4–L5 discs was used to construct maps of tears in each slice and record other features of interest. A template was used to classify data for analysis.

Results. Multiple-level analysis detected 20% more tears than in a single disc section. Concentric, perinuclear, and radiating tears often appeared first in the posterior disc and were numerous throughout life. However, rim lesions, transdiscal tears, endplate separations, and Schmorl's nodes were infrequent in young discs. Rim lesions and transdiscal tears markedly increased in the older discs while the other tears showed modest growth. In elderly discs, many tears acquired blood vessels accompanied by nerves capable of transmitting pain. Apart from about 15% of rim lesions, healing of tears by scar tissue was absent. Links between various types of tears result in complex discographic images from older discs and the cavitation of transdiscal tears lead to segmental instability.

Conclusion. Tears in the L4–L5 disc show different patterns of incidence with aging, which can be explained by current biomechanical concepts. Tears may not only perturb disc function and cause segmental instability, but the frequency of neovascularization accompanied by neoinnervation indicates that pain originating within the degenerate disc should not be dismissed as the frequent evidence of bleeding into the tear lumen indicates the susceptibility of the vessels to trauma.

Key words: human L4–L5 discs, tears, age-related, incidence, neovascularization and innervation, segmental instability. **Spine 2007;32:2797–2804**

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Many previous accounts of disc pathology and its association with age published during the 20th Century were phrased in elegant prose, but very few provided useful incidence data on the different types of tear. When data have been provided, they usually have been based on the examination of single midsagittal samples of each disc,[1–10] which inevitably results in the underrecording of tears. Therefore, as with all of the studies on human spines carried out in our laboratory during the past decade, in the present study we have examined multiple parasagittal slices not only to assess the incidence of tear types but also to study the possible evolution of linkages between tears and to ascertain the extent of neovascularization as a key indicator of reparative activity and source of pain. We developed a simple method for the recording of tears in each disc, which enabled us to easily review the tears in 3 dimensions and the L4–L5 disc was studied as it is the disc level which shows the most advanced changes in patients with low back pain[11] and is the disc most prone to failure in torsion.[12]

Methods

Terminology of Tears. Figure 1 shows the names of each tear and the parts of the disc in which they are found.

Preparation of Samples of Discs for Microscopy. Freshly removed intact lumbar spines excised from 40 males 17 to 79 years of age and 30 females 13 to 78 years of age were fixed by immediate immersion in buffered formal-saline. When fixation was complete, each motion segment was isolated by sawing through the midaxial planes of the vertebral bodies. The neural arches and apophyseal joints were then removed for a future study. After decalcification each disc and its 2 attached halves of vertebral body was cut into 5-mm-thick parasagittal slices to provide up to 10 parallel slices depending on the diameter of the disc. The tissues were processed into wax blocks and 5-μm-thick sections were stained for microscopy.

Recording Disc Tears Using the CrackMap System. The method for recording and tabulating tears is summarized in Figure 2.

Data Organization and Statistics. The findings in the 70 L4–L5 discs were partitioned into 3 age groups: 10 to 30 years (n = 19; 10 male, 9 female), 31 to 50 years (n = 21; 12 male, 9 female), and 51 to 80 years (n = 30; 18 male, 12 female) because some degree of turgescence is retained up to the age of 30 years after which the disc center becomes dry and tears occur with increasing frequency. The age of 50 years signals the arrival of the destructive TDT, linkages developing between tears, and neovascularization.

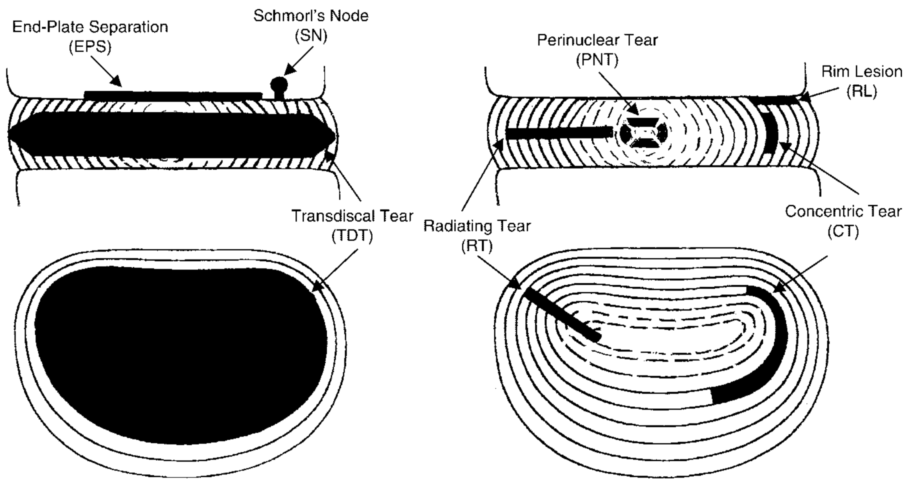


Figure 1. Diagram showing the terminology and text abbreviations for the tears studied together with their characteristic locations in the disc.

Nonparametric methods were applied to determine statistical differences and correlations were calculated using the coefficient of determination (r^2).

■ Results

Incidence of Tears

Table 1 shows that determination of tear incidence by examination of a single midsagittal sample of the L4–L5 disc would have resulted in an overall underrecording of tears by 20%.

There was a highly significant correlation between patient age and total CrackMap score ($r^2 = 0.2086$; $P < 0.00006$) (Figure 3), which confirms that the extent of the disc involved by tears increases progressively throughout life in a linear fashion irrespective of the size or number of tears in a specified zone or, it seems, the order in which the tears make their appearance.

From a young age, CT, PNT, and RT showed a high incidence (Figure 4). First to appear were CT in the outer region of the posterior anulus at the junction between the outer narrow band of thicker lamellae and the inner thinner lamellae forming the bulk of the anulus. PNT were next to form at the upper and lower borders of the nucleus, closely followed by posterior RT which sometimes began as extensions of the PNT (Figure 5). These 3 tears often appeared in the posterior disc before any tear appeared in the anterior anulus.

The remaining tears showed a low incidence in young discs (Figure 4) and while EPS and SN showed a small increase with ageing, RL increased progressively to become frequent in the elderly and TDT were rarely encountered outside the elderly group.

Anterior and Posterior Radiating Tears

Posterior RT were present in 68% and anterior RT in 47% of the 10- to 30-year age group with both types increasing thereafter so that more than 75% in the 51- to 80-year age group contained anterior RT and nearly 90% had posterior RT. Linkages to PNT occurred with 19% of anterior RT and 42% of posterior RT (Figure 5).

Transdiscal Tears

Rare before the age the age of 50 years, TDT were present in 50% of elderly discs and the CrackMaps showed that in the 18 discs with TDT axial cavitation involved 10% of the disc area in 2; 20% in 5; 30% in 5; 40% in 2; 50% in 3; and over 70% in 1 disc. The main channel of TDT often showed "bottle brush" subsidiary fissures (Figure 6) and frequently became linked to RT and CT (Figure 7).

Neovascularization of Radiating Tears and Transdiscal Tears

Neovascularization did not involve anterior RT at any age or other tears before the age of 50 years and after which it was present in 14% of posterior RT and 39% of TDT (Table 2). All posterior RT and the majority of TDT acquired their vascular supply from the posterior disc with the exception of 2 TDT, which acquired vasculature from both posterior and anterior disc regions, and 1 TDT from the anterior region alone.

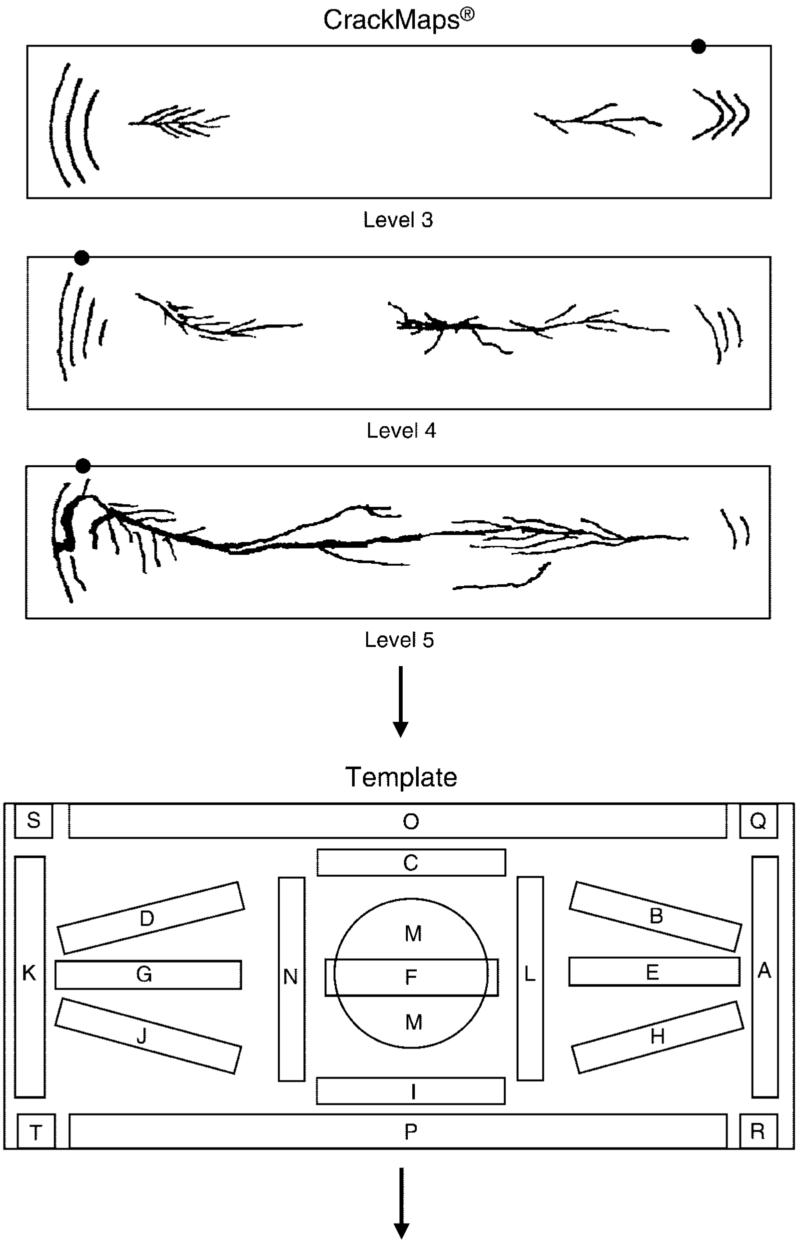
In addition to new blood vessels surrounding tears, they also extended over the inner surfaces of tears with vessel walls often composed only of a single layer of endothelial cells (Figure 8). The finding of red blood cells, fibrin clot, and hemoglobin-derived pigment within tears showed that bleeding had occurred within 80% of the neovascularized tears. Despite neovascularization, there was no evidence of successful repair by scar tissue formation within TDT or RT.

Concentric Tears

In all 3 age groups, CT were present within the anterior anulus in 75% and the posterior anulus in about 100% of discs.

While many anterior CT became linked with anterior RL, there were fewer links between posterior RT and posterior RL and not until after the age of 50 years (Table 3).

Neovascularization occurred less frequently in CT compared with all other tear types and was observed more often when CT extended close to a vertebral rim having a vascularized RL or RT. The dearth of interla-



CrackMap® Score Sheet

Case Code No.	M or F	AGE	FEATURE PRESENT = 1 FEATURE ABSENT = 0																				Total features present
			A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	T	
1																							
2	M	20	1	1	1	0	0	1	0	1	1	0	1	0	0	1	0	0	0	0	0	0	8
3	M	20	1	1	0	1	0	1	0	1	0	1	1	1	1	0	0	0	0	0	0	0	9
4	M	20	1	1	1	0	1	0	0	1	1	0	1	0	1	0	0	0	0	0	0	0	8
5	M	21	1	0	1	0	0	0	1	0	1	1	1	1	1	1	1	1	0	0	0	0	11
6	M	23	1	1	1	0	0	0	0	1	1	0	1	1	0	1	0	0	0	0	0	0	8
7	M	27	1	1	0	0	1	0	1	1	1	0	1	0	0	1	0	0	0	1	1	0	10
8	M	27	1	1	1	1	0	0	0	1	1	0	1	0	0	0	1	0	1	1	0	0	10
9																							

Figure 2. The 3 stages for recording tears: (1) tears in microscope slides from each parasagittal slice entered as CrackMaps; (2) template allocates tears to 20 disc sectors; (3) presence (=1) or absence (=0) of tears entered into 20-column table and the positive entries summated to provide a CrackMap score.

mellar scar tissue in the anulus indicated that healing of CT is unlikely.

Rim Lesions

There was a close correlation between the progressive increase in the incidence of RL with age (r = 0.9997; $P < 0.01$) due not only to an increase in the number of discs developing RL but also to an increase in the number of RL present in each L4–L5 disc. Of the 39 discs containing RL, 10 discs contained 1 RL, 20 contained 2 RL, 3 contained 3 RL and 6 contained 4 RL: 33% of RL were located in the anterior superior rim,

Table 1. Incidence of Intradiscal Tears Not Identifiable by Examination of a Single Mid-sagittal Slice of the L4–L5 Disc From 70 Spines

Tear Type	Concentric Tear	Anterior Radiating	Posterior Radiating	Transdiscal Tear	Rim Lesion	Endplate Separation
Total tears present	68	46	56	18	39	11
Tears not in mid-sagittal slice	3	4	10	5	19	7
Percentage of "missed" tears	4%	9%	18%	28%	49%	64%

25% each in the posterior superior and anterior inferior rims, and 17% in the posterior inferior rim.

RL were classified microscopically into 5 subtypes:

- The cleft type (50%) comprised a transverse break in the anulus lamellae close to their attachment to the bone of the vertebral rim.
- The scar/healing type (20%) comprised a cleft-type RL having granulation tissue within the cleft or a clearly demarcated scar composed of mature fibrous tissue.
- The cystic type (13%) comprised 1 or more dilated cavities having a smooth lining and sometimes showing ingrowth of granulation tissue.
- The fragmented type (13%) comprised a well-defined area showing the breaking up of the attachment zone into multiple randomly arranged portions.
- The vasoproliferative type (5%) consisted of a well-circumscribed area exhibiting a rich meshwork of small blood vessels.

While links between the cavities of RL and RT were infrequent before the age of 50 years, subsequently, 46% of anterior and 36% of posterior RL communicated with anterior and posterior RT, respectively (Table 3). 19% of TDT also developed links to RL and some to CT in the older age group.

Endplate Separations

EPS were present in 10% of the 10- to 30-year age group, 19% of the 31- to 50-year age group, and 17% of the 51- to 80-year age group. Almost equal numbers of L4–L5 discs showed separations involving both upper and lower endplates, or upper or lower endplates alone.

Schmorl's Nodes

The average CrackMap score for discs with SN was about 1 point higher (*i.e.*, had 1 more disc sector with a tear) than discs lacking SN. Present in nearly 20% of discs before the age of 30 SN increased to be present in over 30% of older spines. Three fourths of SN were located in the upper endplate and 75% of SN showed encasement of the herniated portion by a shell of reactive bone formation.

Discussion

Our finding that posterior CT were consistently the first tears to appear is in agreement with the comprehensive study by Hirsch and Schajowicz[5] who reported that concentric "cracks" exist frequently from the age of 15 and are rarely absent after the age of 30. They also described changes in the interlamellar matrix which precede CT formation, subsequently called "delamination."[13]

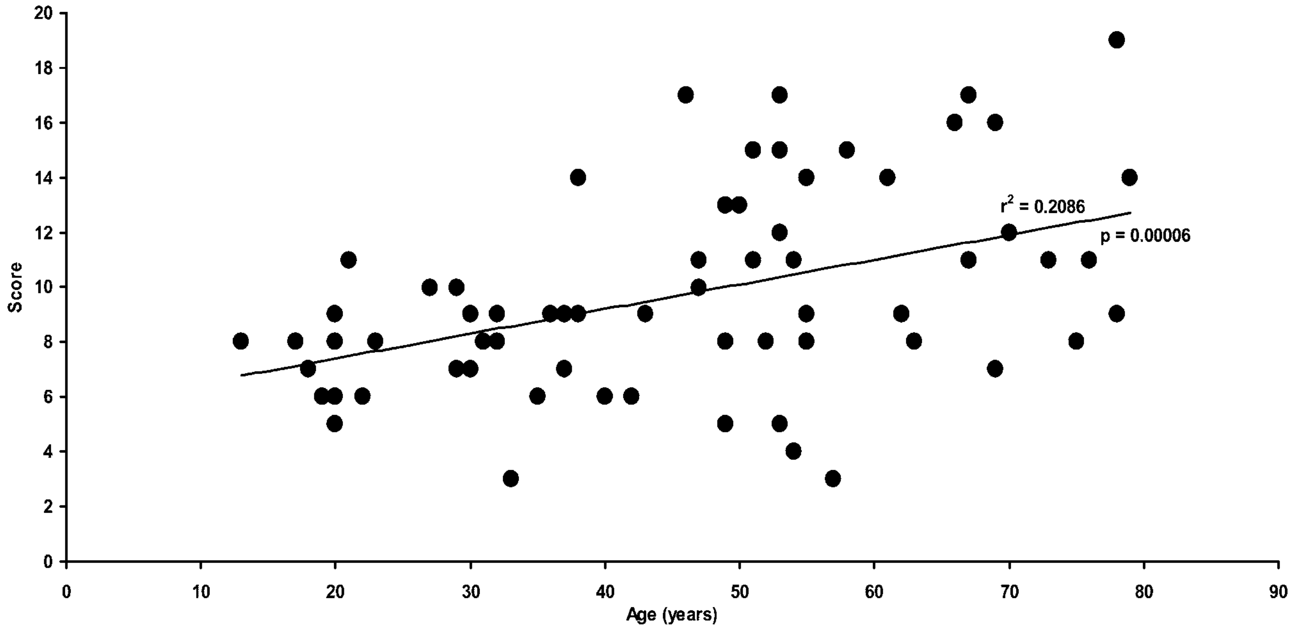


Figure 3. Graph showing the highly significant correlation between age and the unweighted CrackMap score for 70 L4–L5 discs.

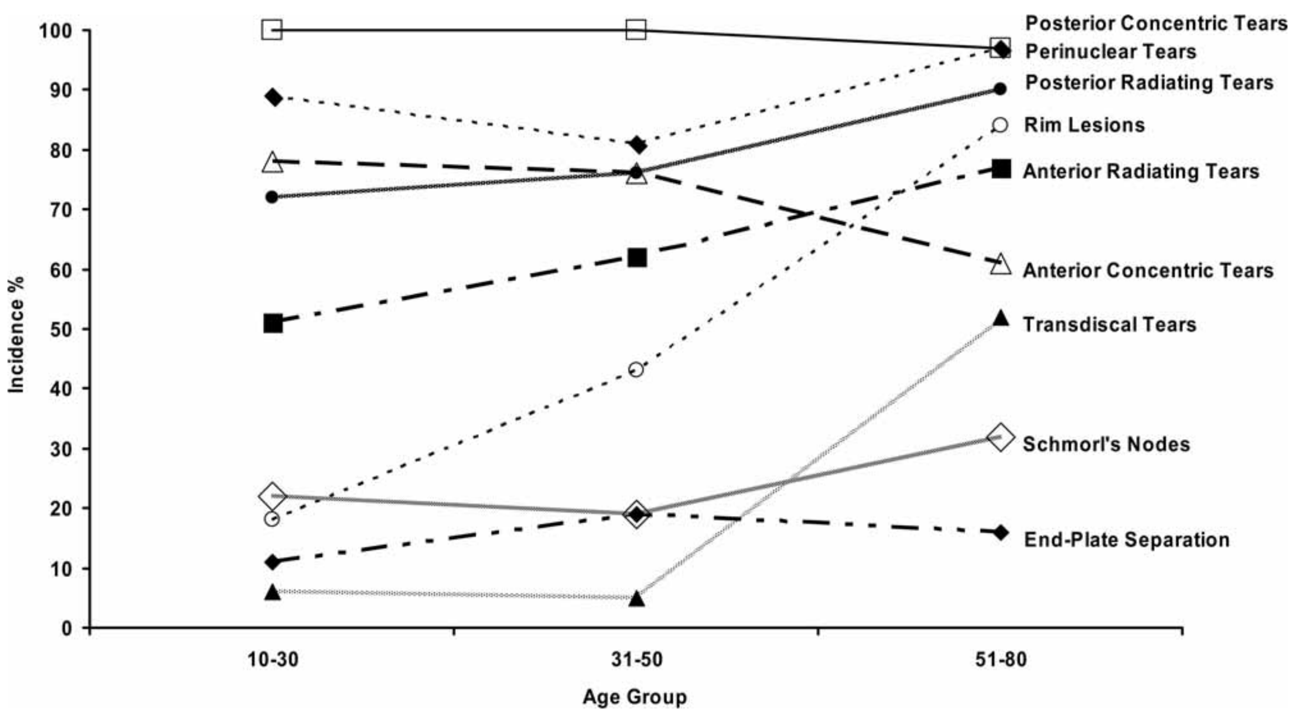


Figure 4. Graph showing percentage incidence of each type of tear in the L4–L5 disc in 3 age groups.

There are substantial differences between the lamellar structure of the anterior and posterior anulus consistent with a dominantly compressive role for the outer anterior anulus and a major tensile role for much of the inner posterior anulus. This is consistent with the lamella being the basic tensile-structural unit and the significantly lower tensile moduli of the posterolateral lamellae is in keeping with the higher frequency of failure in that area of the disc.[14] While posterior CT are the first tears to appear, in both the anterior and posterior anulus CT mostly occur close to the periphery at the inner border of the narrow band of outer and thicker lamellae. Relevant to this finding, Galante[15] concluded that the outer anulus behaved differently from the inner layers, and it has subsequently been shown that the anulus functions in a situation of near uniform hoop stress as its outer region is stiffer than its inner region and this arrangement maintains the stiffness in the presence of an intact anulus when the disc is loaded in compression.[14] Hoop stress exists in the disc despite the fact that at least 40% of the anulus layers are incomplete, especially in the posterolateral disc.[16] While differences in stiffness may be attributed to the outer anulus having a predominance of Type I collagen, whereas Type II collagen dominates the inner layers,[17,18] it has been postulated that intact anular fibers are more important than the facet joints in resisting axial rotation so that a combination of axial stress and torsional stress may result in anulus damage and disc degeneration.[19]

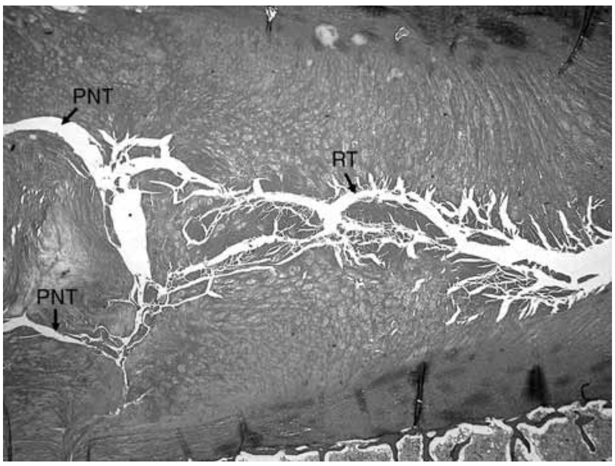


Figure 5. Medium-power microscopic image of sagittal section of the L4–L5 disc from a 54-year-old woman, showing the linkage between upper and lower perinuclear tears (PNT) and a radiating tear (RT). Hematoxylin and eosin, original magnification ×40.

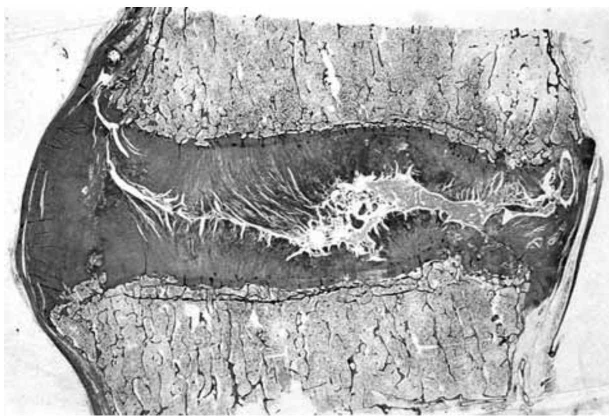


Figure 6. Low-power microscopic image of a sagittal section of the L4–L5 disc from a 72-year-old man, showing a transdical tear with characteristic destructive cavitation of the disc center containing free fragments and the radiating "bottle-brush" pattern of minor clefts. Hematoxylin and eosin, original magnification ×5.

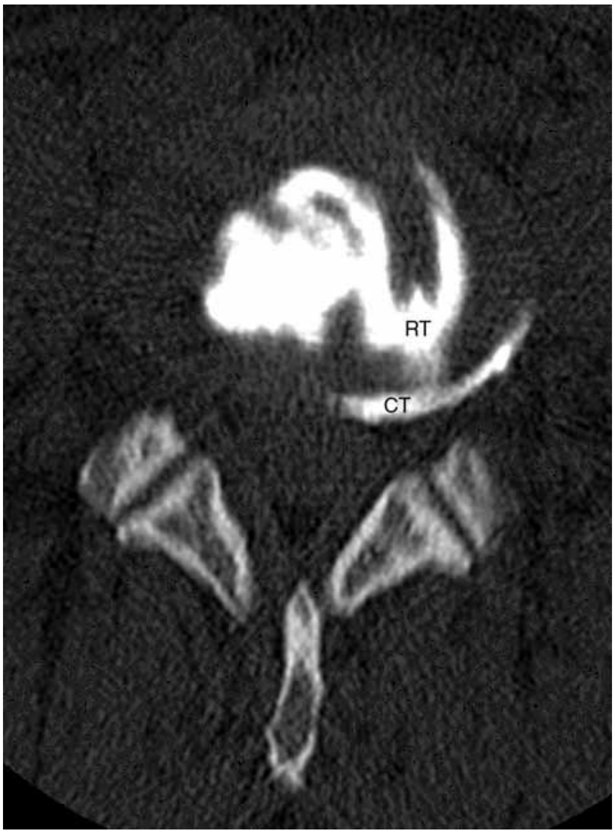


Figure 7. A postdiscography CT scan of the L4–L5 disc in a 60-year-old woman following a right-sided intradiscal injection of contrast shows contrast within a radiating tear (RT), which is linked to a concentric tear (CT) in the outer left posterolateral anulus.

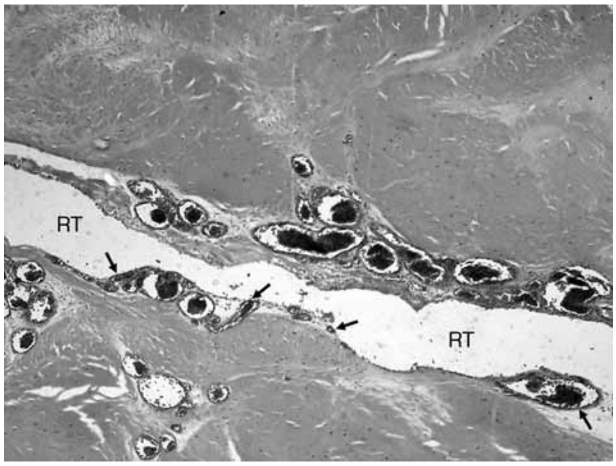


Figure 8. High-power microscopic image of neovascularization of a radiating tear (RT) in the L4–L5 disc showing that some vessels attached to the inner surface have walls composed only of a single layer of endothelial cells (arrows). Hematoxylin and eosin, original magnification ×500.

The importance of maintaining uniform hoop stress is emphasized by the findings in a sheep model of a RL in which a partial-thickness incision into the anulus progressed to advanced disc degeneration.[20] The severing of outer anular fibers in that model would have compromised hoop stress integrity leading to advanced disc failure whereas a different model of a CT in the sheep, induced by an interlamellar injection of fluid unlikely to have any effect on hoop stress, did not result in advanced disc degeneration or more marked degeneration than that induced by needlestick alone.[21]

While posterior CT consistently were the first tears to appear, the center of the disc showed early deterioration

Table 2. Incidence of Neovascularization and Source of Ingrowing Blood Vessels in Radiating and Transdiscal Tears in L4–L5 Discs Over Age of 50 Years

Type of Tear	Percentage Tears With Neovascularization	Percentage Source of Ingrowing Blood Vessels		
		Anterior	Posterior	Anterior and Posterior
Anterior radiating	0	0	0	0
Posterior radiating	14	0	100	0
Transdiscal	39	14	43	43

with PNT appearing commonly during adolescence and with both anterior and posterior RT forming by extension of the axial arms of the PNT in many instances. Our findings agree with those of Friberg and Hirsch[11] who reported that radiating tears invariably start from within the nucleus before extending radially.

In common with other authors,[5,22] we observed the ingrowth of vascularized reparative tissue and agree with their conclusion that minor cracks or parts of larger tears may be filled by scar formation but complete healing of large tears is not possible owing to constant motion between the tear margins. Before the present study, we and other authors have not distinguished TDT from anterior and posterior RT. While Hirsch and Schajowicz[5] reported the incidence of neovascularization in the posterior anulus of L4–L5 to be 40% in their oldest group, this is probably not greatly different from our finding of neovascularization in 14% of posterior RT and 39% of TDT in the same age range. Importantly, Hirsch and Schajowicz[5] postulated that discogenic pain could be attributed to nerves within the ingrowing reparative tissue after concluding that nerves were bound to exist in the vessels and could be the source of pain. We have previously reported the presence of nerves accompanying neovascularization of tears,[23] and it has now been confirmed that nerves immunoreactive for PGP9.5 and substance P accompany the ingrowing blood vessels within discs undergoing neovascularization.[24]

The tears that we have designated as TDT include those which Friberg and Hirsch[11] illustrated as having a "characteristic configuration" of extensive destruction, which was associated with roentgenologically demonstrable "instability" in the form of excessive mobility at the level of the affected disc. The frequent presence of osteophytes arising from the anterior and lateral vertebral rim and the finding of polished disc fragments within TDT[25] adds weight to the concept of

Table 3. Percentage Incidence of Connections Established Between Different Types of Tears in the L4–L5 Disc

Age Group (yr)	Anterior RL to Anterior CT	Posterior RL to Posterior CT	Anterior RL to Anterior RT	Posterior RL to Posterior RT	PNT to Anterior RT	PNT to Posterior RT	TDT to RL
10–30	50	0	11	8	6	22	0
31–50	67	0	0	6	10	33	0
51–80	75	25	46	36	19	42	19

RL indicates rim lesion; RT, radiating tear; PNT, perinuclear tear; TDT, transdiscal tear; CT, concentric tear.

segmental hypermobility resulting from progressive cavitation.

While RL may be unique by virtue of the fact that they are singularly capable of leading to advanced disc degeneration in experimental animals,[20] discs do not require RL as an essential prerequisite to undergoing degeneration. We found RL to be present in 20% of the 10- to 30-year age group, and there was a linear increase thereafter so that they were found in nearly 90% of L4–L5 discs in the group aged 51 to 80 years. The overall incidence of 56% was identical with a previous study of multiple parasagittal samples from 19 and 50 years,[26] and similar to the overall incidence of 63% in spines 30 to 49 years of age and 97% in spines aged over 50 years reported by Hilton and Ball.[4] The most significant difference between our studies and those of Hilton and Ball[4] is the almost complete lack of rim lesions in spines before the age of 30 years reported by those authors and their presence in 20% of our spines at 30 years. The latter difference may be the result of Hilton and Ball[4] examining single midsagittal slices as we have found that rim lesions are more frequently observed in the anterolateral and posterolateral rim zones and occur at a much lower frequency in the midline.

While the early accounts of RL noted the presence of reparative tissue but without successful healing[10] filling of the defect with scar tissue was reported to be present in 7% of anterior RL in a later study.[4] In the present study, we have classified the RL into 5 subtypes, 20% of which were cleft-type rim lesions with reparative tissues; and successful filling of the defect by mature scar tissue had occurred in 15%. We postulate that the cystic, fragmentation, and vasoproliferative types would result in similar weakening of the anular attachment as the more frequent cleft type, and it is possible that the vasoproliferative lesion represents an aberrant or exaggerated reparative response dominated by a profusion of small vessels.

Seeking an explanation as to why the rim attachment zone of the outer anulus is susceptible to failure by a process that microscopically appears to be sudden and traumatic and not a drawn out degenerative process, Hickey and Hukins[27] concluded that torsion and forward bending are likely to cause anular failure, and Krismer *et al*[19] found that the anulus fibers behave like tendons with torsional stress transmitted to those collagen fibers of the anulus which are angled in the direction of the applied torque.

It has been postulated that the cartilage endplate (CEP) plays a filter-like role in preventing fragments of osmotically active proteoglycans from leaving the disc and thereby retaining solutes at a level that allows continuing disc function.[28] While EPS are usually associated with extensive internal disruption in elderly discs, we found a limited separation in a male aged 21 years. In the present study, and from pathologic examination of surgically excised disc protrusions containing CEP, we have found that the plane of cleavage is not always located at the junction of the CEP and BEP but sometimes is within the CEP. This conflicts with the conclusions of Inoue *et al*[8,29] who maintain that the CEP is not anchored to the BEP by collagen fibers thus rendering the CEP susceptible to shear forces and avulsion. Our experience of removing the CEP to examine the underlying BEP in a transaxial study of the T12–L1 disc indicated that tight bonding normally existed between the CEP and BEP. Also, we have been unable to confirm Inoue's concept that intact inner anulus fibers continue horizontally within the CEP to form a capsule of fibers surrounding the nucleus zone.

Schmorl's nodes were present in nearly 20% of discs under the age of 50 years and in over 30% of older discs. While higher incidences have been reported,[1,10,22,30] some authors have included endplate lesions without nuclear herniation and studies, which have included the upper lumbar and dorsal spines will reflect the higher incidence of SN in those regions.

■ Key Points

- All types of disc tear are defined and their age-related incidence in L4–L5 determined.
- A method is described for mapping and recording tears, which enables 3-dimensional reconstruction and analysis.
- While there is a high incidence of tears below the age of 30 years, highly destructive transdiscal tears become increasingly important and pain-transmitting nerves accompany the ingrowth of vascular repair tissue into tears after the age of 50 years.
- The findings are highly relevant to understanding the pathobiology of age-related disc degeneration, pain arising from within the disc, the interpretation of CT discograms, and segmental instability.

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