

# **Microscopic extent of invasion (Required and Recommended)**

## **Reason/Evidentiary Support**

### **Rete testis**

Rete testis invasion is the direct invasion of tumour into the stroma of the rete testis and does not include pagetoid spread of germ cell neoplasia in situ (GCNIS) into the tubules of the rete.<sup>1</sup> In the pooled cohort surveillance study of pure seminomas, rete testis invasion was independently predictive of recurrence at five years on multivariate analysis, conferring an increased risk of recurrence by a factor of 1.7 (95% Confidence Interval (CI) 1.1–2.6)).<sup>1</sup> Other studies of pure seminoma show differing results. Two cohort analyses of 425 and 744 patients respectively confirmed this.<sup>2,3</sup> However, two other studies of 685 patients<sup>4</sup> and 1954 patients<sup>5</sup> showed that rete testis invasion was not a significant predictor for relapse when compared with tumour size.

For non-seminomatous germ cell tumours (NSGCTs), there is less evidence that rete testis invasion is an important prognostic factor,<sup>6</sup> probably because other factors such as the percentage of embryonal carcinoma and vascular invasion are more important.

Rete testis invasion and tumour size are also interdependent. It should be noted that most of the studies listed above did not include formal prospective pathological review and were a retrospective assessment of pathological reports by clinicians. Data on rete testis involvement was missing in many cases, and there is doubt in some studies whether pagetoid invasion of the rete was assessed. A survey of recent practice in Europe showed many pathologists did not distinguish between pagetoid and interstitial invasion of the rete.<sup>7</sup> Rete testis and tumour size were not part of the TNM 7<sup>th</sup> edition<sup>8,9</sup> however tumour size using a cut off of 3 cm has now been incorporated into the American Joint Committee on Cancer (AJCC) 8<sup>th</sup> edition<sup>10</sup> for pure seminomas only, separating the pT1 stage into pT1a and pT1b. Both rete testis invasion and size are used by many clinicians to determine adjuvant chemotherapy and are part of existing European clinical guidelines.<sup>11,12</sup>

### **Hilar soft tissue invasion**

Invasion of the hilar soft tissues is a common mode of extratesticular spread.<sup>13</sup> One study has shown that it predicts high stage at presentation,<sup>6</sup> but there has been previously no consensus on the correct way to stage hilar soft tissue invasion.<sup>7</sup> Following a consultation conference by the International Society of Urological Pathologists (ISUP)<sup>14</sup> and adoption by the AJCC 8<sup>th</sup> edition<sup>10</sup> it has been decided to stage soft tissue invasion as pT2. Soft tissue invasion has been defined as ‘invasion of the adipose tissue and soft fibrous connective tissue present...beyond the boundaries of the rete testis.’<sup>10</sup>

### **Epididymal invasion**

There is no evidence on the prognostic significance of epididymal invasion. Although in previous editions of AJCC<sup>8</sup> and Union for International Cancer Control (UICC)<sup>9</sup> manuals (7<sup>th</sup> editions) it has been designated as pT1, the evidence and consensus for pT2 staging of soft tissue has necessitated a

redesignation of epididymal invasion as pT2 in the AJCC 8<sup>th</sup> edition<sup>10</sup> as it is normally secondary to this.

### **Direct invasion of the cord**

This is regarded as a core data item as it is required for TNM staging but evidence on its prognostic significance in seminoma is lacking. In a large cohort study of stage I seminoma, spermatic cord invasion was not found to be independently prognostic for recurrence.<sup>2</sup> In contrast, it was identified as an adverse prognostic factor in another study.<sup>15</sup> In a review of 326 testicular germ cell tumours, of which 79 had tumour in the spermatic cord, most cases (72%) were thought to be due to contamination compared to 19% cases of true involvement and with 8.9% showing both contamination and true involvement.<sup>16</sup> Spermatic cord contamination was most frequently seen with seminomas. To differentiate cord invasion from hilar soft tissue invasion, it has been defined as 'tumour extending beyond the angle between the epididymis and spermatic cord proper or tumour surrounding the vas deferens'.<sup>10</sup>

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