INTRODUCTION

Since 1993, the incidence of clinical T3 prostate cancer has been reported to be <10% of all newly diagnosed cancers annually (1). However, prior to the era of PSA screening, clinical T3 cancers comprised nearly 20–30% of all newly diagnosed prostate cancers (2,3). In the pre-prostate-specific antigen (PSA) era, treatment outcomes of clinical T3 cancers frequently involved an initial monotherapy approach (either radical surgery or radiation therapy [RT]) with subsequent salvage of a monotherapy failure with a secondary therapy. Analysis of the results from this era using PSA as evidence for biochemical failure revealed unexpected high failure rates for monotherapy treatments. More recently, owing to detailed pathologic examination and the knowledge gained from using PSA to monitor outcomes, an appreciation of the limitations of the monotherapy approach has evolved. The recent momentum has encouraged the use of early, multimodality treatment in the treatment of locally invasive or clinical T3 cancer. The scope of this chapter will encompass the following:

1. A contemporary classification of clinical and pathologic T3 cancer.
2. The most recent data in the treatment of clinical T3, relative to the various risk groups in the contemporary classification of T3 cancers.
3. Recent data on the expanding role of adjuvant hormonal therapy (AHT).
4. A critique of secondary therapies (or salvage therapies), which have been used to treat monotherapy failures of these locally invasive cancers.
#### Table 1

**Current Clinical Staging of Locally Advanced Prostate Cancer**

<table>
<thead>
<tr>
<th>AJCC stage</th>
<th>AUA stage</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>T3a</td>
<td>C</td>
<td>Unilateral extracapsular extension</td>
</tr>
<tr>
<td>T3b</td>
<td>C</td>
<td>Bilateral extracapsular extension</td>
</tr>
<tr>
<td>T3c</td>
<td>C</td>
<td>Seminal vesicle invasion</td>
</tr>
<tr>
<td>T4</td>
<td>C</td>
<td>Adjacent organ invasion</td>
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*AJCC, American Joint Committee of Cancer; AUA, American Urological Association.

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#### DEFINING AND STAGING LOCALLY INVASIVE PROSTATE CANCER

**Staging Clinical T3 Cancers**

Interpreting the data surrounding treatment of locally invasive prostate cancer is challenging because of the changing definition of what is locally invasive cancer or clinical T3 cancer. Various clinical definitions and impressions can dramatically alter the tumor volumes compared, the extent of extracapsular disease, and the outcomes from treatment. The classical definition of locally invasive prostate cancer is palpable gross extracapsular extension into the seminal vesicles either unilaterally or bilaterally. This is the classic stage C prostate cancer as defined by our current staging systems (Table 1).

However, as annual PSA and digital rectal examination (DRE) screening have matured, we detect fewer classic stage C cancers, and more commonly, we palpate unilateral induration of the capsule with questionable extension into the seminal vesicle. These cancers are still categorized as clinical T3 cancers, but have considerably less tumor volume than the classical stage C cancers. In fact, we often question our DRE on these cancers, knowing the clinical overstaging error for seminal vesicle invasion can be as high as 20% (4). Our ambivalence on the clinical exam is reflected in the prior literature, which often combines the clinical stages B2 and C, as B2/C. The other notable variant of a clinical T3 cancer is the palpable nodule located in the peripheral zone at the apex or midgland that obscures the sulcus and is extracapsular, but does not extend into the seminal vesicles. This lesion is a clinical T3, but has even less tumor volume than a B2/C lesion, and will have a better outcome with treatment than a clinical C with seminal vesicle invasion.

**Staging Pathologic T3 Cancers: Integration of PSA and Gleason Scores**

The correlation of clinical staging with tumor volume for locally invasive prostate cancer is less than ideal and only recently, with the integration of PSA and Gleason scores, have we been able to stratify these tumors better. Detailed review of the pathologic specimens from patients undergoing radical prostatectomy (RP) has informed us that many cancers thought to be organ-confined on clinical staging were actually pathologic T3 cancers (or tumor extending beyond the capsule or into the seminal vesicles). The incidence of pT3 cancers as stratified by initial PSA is seen in Table 2 (5), where nearly 70% of the patients with an initial PSA < 10 had at least focal extracapsular extension. Similarly, as shown in Table 3, when stratified by biopsy Gleason score, roughly 55% of