OBJECTIVE
To compare the clinical and surgical findings using translabial ultrasonography (US) in the evaluation of symptoms after transvaginal synthetic mesh placement.

METHODS
From 2009 through 2010, a retrospective observational study was conducted to evaluate patients presenting with complaints after transvaginal mesh implantation for the treatment of stress urinary incontinence or pelvic organ prolapse repair. The clinical and translabial US findings were compared with the intraoperative findings, with a focus on mesh location, erosion, and extrusion.

RESULTS
A total of 51 consecutive patients (mean age 59 years) were evaluated by history and physical examination, translabial US, and intraoperative findings. Using intraoperative findings as the reference standard, translabial US was able to predict the location of the sling in relationship to the urethra (6 distal, 25 mid-urethral, and 20 at the bladder neck), to differentiate between transobturator (n = 21) and retropubic (n = 30) slings, and to detect all anterior (n = 21) and posterior (n = 15) placed mesh. Translabial US was superior to physical examination in identifying mesh erosion into the periurethral fascia or sphincteric unit. US was inferior to physical examination in diagnosing vaginal extrusion but was superior for locating the mesh.

CONCLUSION
Translabial US can identify the mesh material used to treat stress urinary incontinence and pelvic organ prolapse. It provides additional information on sling type, mesh location, and morphology compared with the clinical findings and could help in surgical planning and counseling. Prospective clinical studies evaluating the reliability of this technique in larger patient populations are warranted.

MATERIAL AND METHODS
Patient Selection and Evaluation
A retrospective observational study was conducted of consecutive patients, who had undergone surgical exploration for stress urinary incontinence (SUI) and pelvic organ prolapse repair. The clinical and translabial US evaluation of symptoms after transvaginal synthetic mesh placement.

In the past decade, an increase has occurred in the use of transvaginal synthetic mesh for the treatment of stress urinary incontinence (SUI) and pelvic organ prolapse (POP). Mesh implantation is not completely free of complications and can include erosion, extrusion, infection, pain, irritative voiding symptoms, and recurrence of prolapse or incontinence. Major complications, such as urethral and bladder perforation, can occur, can present with only mild urinary symptoms, and are often missed on clinical evaluation. A number of factors limit the surgeon’s ability to predict the intraoperative findings when surgery is needed to remove the mesh: (1) the operative records can be missing or lack detail of the approach used, (2) the mesh can change, making it difficult to locate, (3) bladder or urethral erosion can be subclinical and could be missed on cystoscopy, and (4) on physical examination, it can occasionally be challenging to evaluate patients with a history of partial or complete mesh removal, in which case, the remaining mesh could account for a patient’s persistent symptoms. Therefore, improved diagnostic tools are needed to improve patient care and aid in surgical planning.

Synthetic mesh cannot be properly visualized using radiography, computed tomography, or magnetic resonance imaging. Magnetic resonance imaging requires spinning hydrogen atoms for image construction and is therefore not a good modality for detecting plastic foreign material such as synthetic mesh. However, the mesh is highly echogenic, making ultrasonography (US) an effective imaging method.

Because no larger studies have yet been published of patients presenting with complications after mesh placement for SUI and POP, the aim of the present study was to understand the ability to detect mesh on clinical examination and translabial US compared with the intraoperative findings.

Financial Disclosure: The authors declare that they have no relevant financial interests.

From the Division of Pelvic Medicine and Reconstructive Surgery, Department of Urology, Loma Linda University School of Medicine, Loma Linda, CA; the Department of Radiology, University of California Los Angeles, David Geffen School of Medicine, Los Angeles, CA; and the Division of Pelvic Medicine and Reconstructive Surgery, Department of Urology, University of California Los Angeles, David Geffen School of Medicine, Los Angeles, CA.

Reprint requests: Andrea Staack, M.D., Ph.D., Division of Pelvic Medicine and Reconstructive Surgery, Department of Urology, Loma Linda University School of Medicine, Faculty Medical Offices, 11370 Anderson Street, 1100, Loma Linda, CA 92354. E-mail: astaack@llu.edu

January 2009 to September 2010 to address bothersome de novo symptoms after placement of transvaginal mesh.

All patients underwent an initial physical examination by the same examiners, who were evaluating for mesh position and extrusion, and were offered a translabial US evaluation. The present cohort included only those patients who underwent a translabial US examination preoperatively. A radiologist (N.R.) evaluated the US scans and helped to develop the protocol.

Intraoperative findings were recorded in the operative note by the primary surgeon at surgery and were noted using a standardized method by 1 of us (A.S.). Surgical documentation reported the intraoperative findings from vaginal inspection and urethrocystoscopy, followed by the findings on the location of the central aspect of the sling (in relationship to the urethra or bladder neck) and the sling arms (in relationship to the obturator foramen or retropubic space). If applicable, findings on the position and morphology of anterior and posterior vaginal mesh were reported.

Comparisons of the clinical, US, and surgical findings were done after all reported patients were treated. The institutional review board approved the present retrospective study.

**Translabial US Technique**

**Patient Preparation and Positioning.** The patients were positioned supine, with the knees flexed and the hips abducted. The pelvic tilt was improved by placing a pillow or wedge under the pelvis. The patients had been asked to empty their bowels before the examination and to keep the bladder moderately full to enhance the image quality.

**Transducer Selection.** A transvaginal transducer can be used to evaluate the pelvic organs. To decrease the discomfort and invasiveness of the US evaluation, a curvilinear transducer applied externally to perineum and labia has been more commonly used. The curvilinear transducer is routinely used for transabdominal renal or bladder evaluation and is readily available in most urologic practices.

For evaluation of the mesh, the transducer was placed at the perineum in close proximity to the introitus. Frequencies of 5-9 MHz provided an optimal resolution of the pelvic floor anatomy and for mesh visualization at the anterior (AVW) or posterior vaginal wall (PVW). The transducer was covered with a powder-free glove for hygienic precautions. Scanning was done with minimal pressure to prevent organ movement, thinning of nearby structures, shifting of implants, and discomfort. Assessment of the pelvic floor using translabial US was conducted in 3 phases: (1) static 2-dimensional studies, (2) dynamic cine evaluation with coughing and Valsalva maneuvers, and (3) 3-dimensional (3D) reconstructions. For the present study, the iU22 system from Philips Healthcare (Best, The Netherlands) was used.

**Identification of Anatomic Landmarks With 2-Dimensional Translabial US Studies.** Bony structures and mesh are hyperechogenic and thus will appear “light” or “white” compared with urine and gas. Important landmarks include the pubic bone, urethra, urethrovesical angle, bladder neck, and rectoanal angle. The midline was defined at the point of the widest diameter of the pubic bone. In the present study cranioventral structures, such as the pubic bone, were documented on the left side of the image and dorsocaudal structures, such as the rectum, were documented on the right side, with the perineum superiorly. For the sagittal view, the transducer was positioned vertically between the labia majora. The midsagittal plane provided views of the entire diameter of the pubic bone, which functioned as a landmark. The urethra, urethrovesical angle, bladder, vagina, and rectoanal angle were assessed in the midline (Fig. 1A). In this plane, the suburethral sling was detected between the urethra and anterior vaginal wall (AVW). The sling was clearly located at its position in relationship to the urethra: distal, midurethral, or proximal at the bladder neck (Fig. 1A-C). Mesh at the AVW or PVW (used for POP repair) was easily identified (Fig. 1D,E).

The coronal plane was obtained by positioning the transducer horizontally and tilting it inward or outwards toward the patient’s head or sacrum, respectively. The landmarks at the coronal plane were the urethra, urethrovesical angle, and bladder. The coronal plane was preferred to distinguish transobturator and retropubic slings. The arms of the sling can be best appreciated in this plane, and the sling type was identified according to the direction of the arms.

By angling the transducer strongly in the horizontal position, we obtained an extremely tilted coronal view. For simplicity, it was referred to as the axial or transverse view. The landmarks were the lumen of the urethra (hypoechogenic), levator muscle (hyperechogenic), and anal sphincter.

**Cine Loop Function With Dynamic Evaluation.** Cine loop features enhance the visualization of the anatomy of interest. Real-time graphics for dynamic maneuvers such as the Valsalva and coughing were obtained and reviewed separately. Dynamic-cine loop studies aided in the identification of the location of the slings and in determining the position of the mesh in relationship to the bladder neck. It also identified urethral hypermobility, urethral kinking, and the presence of anterior, posterior, or apical prolapse.

**3D Reconstruction Studies.** The Philips iU22 system (containing hardware for 4-dimensional, real-time US) was used for the 3D examinations. It was performed using the 3D 9-3 V automated curved transducer, which was placed at the perineum for the examination. When using the 3D-imaging modus for translabial US, 3 different planes (midsagittal, coronal, and axial) were automatically reconstructed without major tilting of the transducer. The axial plane referred to the vertical to both the midsagittal and the coronal planes. 3D imaging was applied to virtually reconstruct the urethra to detect an intramural or extramural mesh position in relationship to the urethra to improve visualization of the mesh fragments (Fig. 1F) and to detect folding of the mesh.

**Statistical Analysis**

All data were retrospectively extracted from the patient charts, US reports, and operative notes, entered in a de-identified database, and quantitatively analyzed using descriptive statistics.

**RESULTS**

**Patient Characteristics**

A suburethral sling had been placed in all patients (n = 51) during previous surgery. Of the 51 patients, 36 (71%) had undergone additional anterior or posterior prolapse repair with mesh and 41 (80%) had been found with mesh extrusion or erosion. All patients underwent a clinical examination, translabial US, and surgical exploration.
The mean period from initial surgical mesh placement to surgical exploration was 3 years (range 1-10). Their mean age was 59 years (range 31-88).

Clinical Findings
All patients presented with a variety of lower urinary tract symptoms (Table 2) and underwent an initial physical examination. During the pelvic examination, it was not possible to accurately determine the synthetic mesh type, sling location, or presence or absence of sling disruption or transection or to distinguish mesh placed for AVW prolapse repair from a suburethral sling (Table 1). On examination, mesh used for AVW prolapse repair was localized in almost all patients and that used for PVW prolapse repair in only one half of the patients (Table 1). Because of scar tissue formation or pain from previous transvaginal surgery, the vaginal examination was sometimes difficult.

The AVW, PVW, urethra, and bladder were evaluated for extrusions and erosions in all patients. The sensitivity was 100% for detecting AVW (including suburethral slings) and PVW extrusions of mesh on physical examination and vesical erosions at cystoscopy (Table 1). Of 7 patients with complete mesh erosion into the urethral lumen, who had presented intraoperatively with urethral mesh erosion, 1 had been diagnosed preoperatively using

Figure 1. Normal position and configuration of synthetic mesh. (A) Anatomic landmarks of distal periurethral sling position in midsagittal plane. The midsagittal view is found at the largest diameter of the pubic bone. At the midsagittal view, the entire urethral length, bladder neck, bladder, vagina, rectum, and rectoanal angle can be visualized. (B) Position of mid-urethral sling in midsagittal plane. (C) Position of proximal suburethral sling at the level of the bladder neck. (D) Anterior vaginal wall (AVW) mesh in a patient with cystocele in sagittal plane. (E) Posterior vaginal wall (PVW) mesh supporting rectal wall for rectocele repair in sagittal plane. (F) Suburethral sling fragments after sling revision in 3-dimensional reconstruction. Arrows indicate mesh. Bl, bladder; R, rectum; S, suburethral sling; U, urethra; V, vagina. (Color version available online.)
urethrocystoscopy (Table 1). Slings penetrating the lumen of the urethra were depicted by cystoscopy, translabial US, and intraoperatively. Slings eroding into the periurethral fascia or sphincteric unit were not recognized during cystoscopy but were found during US evaluation and intraoperatively.

**Evaluation of Synthetic Mesh Implants With Translabial US**

Fewer than one half of all patients (21 of 51, 41%) presented with documented information on the type of previous mesh implantation. Of those 21 patients, 11 (52%) presented with a suburethral sling only, 3 (14%) with a sling plus AVW mesh, and 7 (3%) with a sling plus AVW and PVW mesh. The mesh location was confirmed by translabial US (100% sensitivity).

More than one half of the patient cohort (30 of 51, 59%) did not have previous operative reports available and provided information of limited accuracy about the type and location of their synthetic vaginal mesh implant. Of those 30 patients, translabial US provided the following information on mesh type and location: 18 (60%) were found to have only a suburethral sling, 4 (13%) had a suburethral sling and mesh at the AVW, 7 (23%) had a suburethral sling and mesh at the AVW and PVW, and 1 (3%) had a suburethral sling and mesh at the PVW. For all 51 patients, the mesh location was confirmed intraoperatively.

Translabial US determined the sling position in relationship to the urethra and bladder neck (Fig. 1A-C), distinguished transobturator and retropubic slings, and detected folded or disrupted slings in all patients (100% sensitivity), using the intraoperative findings as the reference standard (Table 1). The retropubic slings appeared as U-shaped structures surrounding the urethra and extending superiorly. Transobturator slings appeared dove-shaped, extending laterally and located at the posterior urethra. The suburethral slings were located at the distal urethra, mid-urethra, and bladder neck (Table 1). In addition to synthetic slings, AVW and PVW mesh was located in all patients using translabial US, with the findings confirmed during surgical exploration.

The urethra, bladder, and vaginal wall were evaluated for mesh extrusion or erosion with translabial US. In the patients presenting with mesh extrusion on physical examination, no extrusion was detected by US (Table 1). Using the intraoperative findings as the reference standard for comparison, all vesical and urethral erosions were found using translabial US (Table 1). Slings penetrating the sphincteric unit, suburethral epithelium, or periurethral fascia were recognized using translabial US compared with direct visualization intraoperatively. 3D reconstructive US was helpful to detect intramural mesh penetration of the urethra in those patients who had presented with irritative voiding symptoms.

**Intraoperative Findings**

All 51 patients with previous surgery for vaginal synthetic mesh placement were symptomatic and underwent surgical exploration and repair. During surgical exploration, the suburethral sling type and location were determined in all patients and confirmed the preoperative US findings (Table 1). All vaginal wall mesh extrusions, bladder and urethral mesh erosions, and folding or

---

**Table 1.** Descriptive analysis of findings of mesh location and morphology during clinical examination, translabial ultrasonography, and intraoperative exploration

<table>
<thead>
<tr>
<th>Mesh Location</th>
<th>Clinical Examination (Including Urethrocystoscopy) Findings</th>
<th>US Findings</th>
<th>Intraoperative Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Suburethral sling* (n = 51)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transobturator</td>
<td>0/21 (0%)</td>
<td>21/21 (100%)</td>
<td>21/21 (100%)</td>
</tr>
<tr>
<td>Retropubic</td>
<td>0/30 (0%)</td>
<td>30/30 (100%)</td>
<td>30/30 (100%)</td>
</tr>
<tr>
<td>Distal</td>
<td>0/6 (0%)</td>
<td>6/6 (100%)</td>
<td>6/6 (100%)</td>
</tr>
<tr>
<td>Mid</td>
<td>0/25 (0%)</td>
<td>25/25 (100%)</td>
<td>25/25 (100%)</td>
</tr>
<tr>
<td>Proximal</td>
<td>0/20 (0%)</td>
<td>20/20 (100%)</td>
<td>20/20 (100%)</td>
</tr>
<tr>
<td>Folding</td>
<td>0/30 (0%)</td>
<td>30/30 (100%)</td>
<td>30/30 (100%)</td>
</tr>
<tr>
<td>Disrupted or transected</td>
<td>0/30 (0%)</td>
<td>30/30 (100%)</td>
<td>30/30 (100%)</td>
</tr>
<tr>
<td>Total</td>
<td>0/51 (0%)</td>
<td>51/51 (100%)</td>
<td>51/51 (100%)</td>
</tr>
<tr>
<td>Pelvic organ prolapse repair* (n = 36)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterior</td>
<td>20/21 (95%)</td>
<td>21/21 (100%)</td>
<td>21/21 (100%)</td>
</tr>
<tr>
<td>Posterior</td>
<td>7/15 (47%)</td>
<td>15/15 (100%)</td>
<td>15/15 (100%)</td>
</tr>
<tr>
<td>Total</td>
<td>27/36 (75%)</td>
<td>36/36 (100%)</td>
<td>36/36 (100%)</td>
</tr>
<tr>
<td>Extrusion or erosion* (n = 41)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterior vaginal wall</td>
<td>25/25 (100%)</td>
<td>0/25 (0%)</td>
<td>25/25 (100%)</td>
</tr>
<tr>
<td>Posterior vaginal wall</td>
<td>7/7 (100%)</td>
<td>0/7 (0%)</td>
<td>7/7 (100%)</td>
</tr>
<tr>
<td>Bladder</td>
<td>2/2 (100%)</td>
<td>2/2 (100%)</td>
<td>2/2 (100%)</td>
</tr>
<tr>
<td>Urethra</td>
<td>1/7 (14%)</td>
<td>7/7 (100%)</td>
<td>7/7 (100%)</td>
</tr>
<tr>
<td>Total</td>
<td>35/41 (85%)</td>
<td>9/41 (22%)</td>
<td>41/41 (100%)</td>
</tr>
</tbody>
</table>

*All patients (n = 51) had a history of synthetic mesh sling placement; of the 51 patients, 36 had undergone pelvic organ repair and 41 had developed mesh extrusion or erosion.
Table 2. Presenting symptoms after treatment with vaginal synthetic mesh for stress urinary incontinence and/or pelvic organ prolapse repair (n = 51)

<table>
<thead>
<tr>
<th>Clinical Presentation</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pelvic pain</td>
<td>37 (73)</td>
</tr>
<tr>
<td>Dyspareunia</td>
<td>31 (61)</td>
</tr>
<tr>
<td>Hematuria</td>
<td>4 (8)</td>
</tr>
<tr>
<td>Vaginal discharge or bleeding</td>
<td>4 (8)</td>
</tr>
<tr>
<td>Lower urinary tract symptoms</td>
<td></td>
</tr>
<tr>
<td>Frequency</td>
<td>30 (59)</td>
</tr>
<tr>
<td>Hesitancy</td>
<td>12 (4)</td>
</tr>
<tr>
<td>Nocturia</td>
<td>24 (47)</td>
</tr>
<tr>
<td>Urgency</td>
<td>31 (61)</td>
</tr>
<tr>
<td>Incontinence</td>
<td>33 (65)</td>
</tr>
<tr>
<td>Dysuria</td>
<td>5 (10)</td>
</tr>
<tr>
<td>Obstructive voiding symptoms with urinary retention</td>
<td>16 (31)</td>
</tr>
<tr>
<td>Recurrent urinary tract infections</td>
<td>11 (22)</td>
</tr>
</tbody>
</table>

disruption were identified during surgical exploration (Table 1, Fig. 1F).

Comparison of Clinical, US, and Intraoperative Findings

The findings from the clinical examination seemed inferior to the US findings or intraoperative mesh localization. The mesh type (placed during previous transvaginal surgery) and folding or disruption could not be detected clinically. The clinical findings, however, of vaginal wall mesh extrusion were superior to the US findings. To detect intramural or transmural sling erosion of the urethra, translabial US was superior to the clinical examination.

The surgeon was aware of the preoperative clinical and US findings. The preoperative knowledge of urethral mesh erosions determined by cystoscopy and US seemed valuable to the surgical exploration and intraoperative localization of urethral and vesical erosion. Surgery confirmed the preoperative US findings of the mesh location and the clinical findings of mesh erosion.

COMMENT

In previous years, patient presentations with complaints after vaginal mesh surgery have increased. Because magnetic resonance imaging and computed tomography are not suitable diagnostic methods for detecting vaginal synthetic mesh material, our goal was to use translabial US to identify vaginal synthetic mesh after anti-incontinence or POP procedures in patients presenting with urinary tract symptoms and to evaluate the sensitivity of translabial US as an aid to diagnose and evaluate mesh complications compared with the clinical examination and intraoperative findings. US has been used to evaluate the pelvic floor anatomy and to identify bladder neck mobility, urethral position, prolapse, and the anatomy of the levator musculature. Dynamic US evaluation has been demonstrated in a number of similar conditions.

The utility of US in evaluating suburethral slings or the synthetic mesh used for POP repair has been reported with a focus on the tension and position of transvaginal tape placement and its outcome. To our knowledge, we are the first to compare the information on mesh location obtained from translabial US with the intraoperative findings. The present study systematically evaluated the US findings and the clinical findings obtained by history and physical examination and compared them with the intraoperative findings. When using the surgical findings as the reference standard, we found that US had 100% sensitivity in determining the sling type (obturator vs retropubic) and the location in respect to the urethra (proximal, distal, bladder neck) and had 100% sensitivity for locating urethral and bladder erosion. Only 2 previous reports with very small sample sizes have described the ability of US in detecting mesh erosion into the urinary tract in the diagnosis of urethral mesh erosion. We found no utility of US to evaluate vaginal extrusion of the mesh.

It has been shown that 3D reconstruction contributes to better visualization of the urethral sphincteric unit. In our study, we used this technique to evaluate suburethral slings in symptomatic patients. We also found 3D reconstruction of the urethra helpful in determining sling folding or suburethral mesh erosion to the submucosa. Dynamic-cine loop studies appeared more useful than static images for determining the sling location in relationship to the urethra and bladder neck using Valsalva and coughing maneuvers.

Although it has been reported that the location of a suburethral sling can affect the outcome of SUI symptoms, no long-term prospective studies have yet been published. It has been reported that slings placed too proximal to the bladder neck or that migrate caudally toward to bladder neck can lead to worse outcomes of symptoms of SUI. It has also been suggested that contraction of the sling material could also contribute to these failures; however, the available data have been contradictory. To date, only limited studies have evaluated mesh morphology and its effect on persistent SUI symptoms or complications. Given that we did not evaluate patients with a good outcome after anti-incontinence surgery using US, we were unable to determine whether the position or mesh shrinkage is important to the outcome. Nevertheless, we found that the US assessed the majority of slings with changed morphology and could easily provide information on mesh location, type, and size (Table 1). Thus, US would be an excellent adjunct to studies evaluating how the sling position and morphologic changes influence outcomes after surgical correction of SUI. In the present cohort, the preoperative findings from US were useful for surgical planning, especially when the type and location of the previously placed mesh were unknown or the patient had a history of mesh revision and/or removal.

The Food and Drug Administration Safety Communication has warned of serious complications associated
with surgical mesh placement for transvaginal repair of POP.\textsuperscript{1} We applied translabial US to identify and locate AVW or PVW mesh used for POP repair in patients presenting with various symptoms (Table 2). Compared with the intraoperative findings, we found 100% sensitivity for US in detecting mesh at the AVW or PVW (Table 1). Identifying mesh using translabial US before surgical exploration seemed helpful increasing the understanding of the etiology of the pain and helped in counseling and treatment of this difficult patient population.

The present study had inherent limitations, including the retrospective nature and that the surgeon was not aware of the previous evaluations. Attempts were made to overcome some of these limitations by reporting the intraoperative observations by an investigator who was unaware of the preoperative evaluation and US findings. Long-term prospective studies randomizing patients to preoperative US vs physical examination alone and evaluating the intra- and postoperative outcomes will more appropriately determine the usefulness of translabial US. In addition, the value of intraoperative, US-assisted, exploration should be evaluated, including the role of intraoperative 3D and/or 4-dimensional US, which could potentially provide greater quality images for real-time intraoperative evaluation.\textsuperscript{10} Despite these previously stated limitations, the present study was meant as a pilot study to assess the potential utility of this radiologic technique in aiding the surgical exploration and removal of mesh.

\section*{CONCLUSION}
Translabial US is a simple, inexpensive, and noninvasive method that was well tolerated by patients with mesh complications. It can be used as an adjunct in the evaluation of patients presenting with vaginal mesh-related complications to determine the sling type, mesh location, and erosion into lower urinary tract organs, especially when previous operative reports are not available, when persistent symptoms occur after mesh removal, or when mesh erosion is suspected in the absence of endoscopic confirmation.

\section*{Acknowledgments} The authors acknowledge Dr. Shlomo Raz’ original idea to use translabial ultrasound to evaluate and localize synthetic mesh and his valuable input to initiate our study. We also thank Jin Chong and Sherry Chanslor from the Department of Radiology at the University of California, Los Angeles, for their technical help.

\section*{References}

Downloaded for Roopa Ram (ramu@uams.edu) at University of Arkansas for Medical Services from ClinicalKey.com by Elsevier on February 05, 2019. For personal use only. No other uses without permission. Copyright ©2019. Elsevier Inc. All rights reserved.


