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MR imaging of cervical carcinoma: comparison among T2-weighted, dynamic, and postcontrast T1-weighted images with histopathological correlation

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Abstract
Background: To identify the reasons for misdiagnosis of the degree of stromal invasion by uterine cervical cancer with various magnetic resonance sequences.
Methods: T2-weighted, dynamic, and postcontrast T1-weighted images were obtained in the sagittal plane in 20 patients with uterine cervical cancer. After evaluating these sequences for the degree of stromal invasion, histologic specimens were directly correlated with these images.
Results: The degree of stromal invasion was correctly diagnosed in 15 of the 20 cases on T2-weighted images, in 12 on dynamic images, and in eight on postcontrast T1-weighted images. All misdiagnoses were due to overestimation. Histologically, peritumoral stroma showed inflammation or edema in two patients, whereas no histological abnormality was found in the other patients. A hyperintense rim, i.e., a peritumoral enhanced ring-shaped structure, was observed on the enhanced images of five patients. The hyperintense rim corresponded to the periphery of the tumor in three patients and to the cervical stroma in two patients.
Conclusion: T2-weighted images permitted the most accurate evaluation of stromal invasion by uterine tumors. Overdiagnosis may be due to an abnormal intensity of the cervical stroma, which was observed more frequently on dynamic and postcontrast T1-weighted images than on T2-weighted images.

Key words: Uterus, cervix, neoplasm—Magnetic resonance, diagnosis.

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Several studies have emphasized the value of magnetic resonance imaging (MRI), especially T2-weighted spin echo (SE) imaging, in evaluating regional extension of uterine cervical cancer because of its high contrast resolution and multiplanar imaging ability [1–6]. Postcontrast T1-weighted SE images have been reported to be inferior to T2-weighted SE images [7]. The accuracy of evaluation of stromal invasion was reported to be 76% with T2-weighted SE images and 38% with postcontrast T1-weighted SE images [8]. The poor results with postcontrast T1-weighted SE images are explained by poor contrast between the tumor and the cervical stroma because they are enhanced to the same degree [8, 9]. Another possible reason is that the stroma surrounding the tumor is enhanced at a higher intensity than the normal stroma, and tumors confined to the cervix are often overdiagnosed [9].

Dynamic MRI has been reported to be more accurate than T2-weighted imaging in diagnosing stromal invasion [7]. The possible reasons are as follows. Tumors are enhanced more intensely than the cervical stroma and the myometrium in the earliest phase of dynamic MRI (30–60 s after Gd-DTPA injection), and the contrast between the tumor and the cervical stroma may be better than that on T2-weighted or late-phase dynamic MR images. However, there has been only one report [7] regarding the usefulness of dynamic MRI. In this study, we evaluated the diagnostic accuracy of stromal invasion on T2-weighted, dynamic, and postcontrast T1-weighted images. Histologic specimens were then directly correlated with these images to identify the reasons for misdiagnosis of the degree of stromal invasion by uterine cervical tumors.

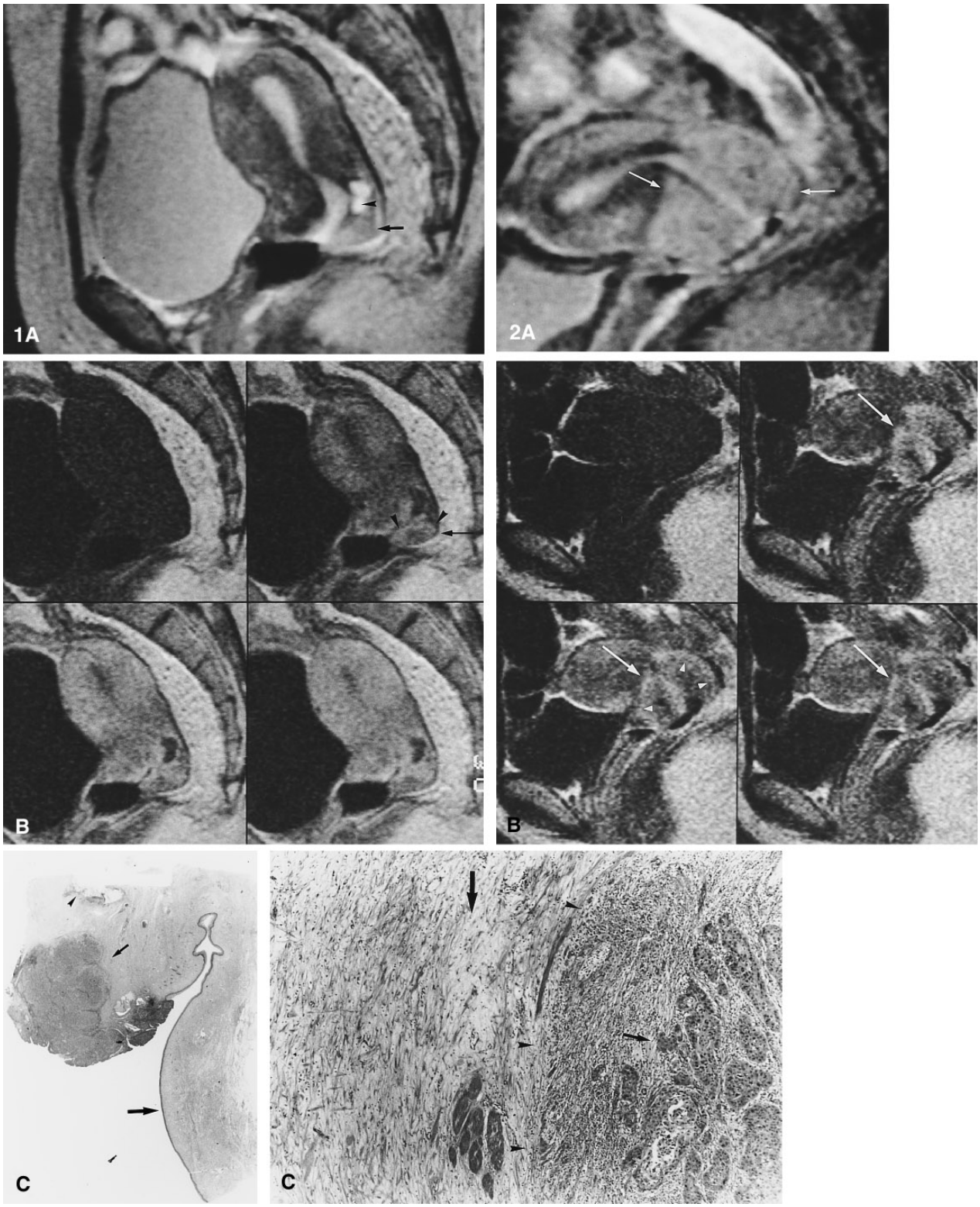

Fig. 1. Cervical squamous cell carcinoma in a 43-year-old woman. **A** Parasagittal T2-weighted MR image shows a small high-intensity lesion in the posterior lip (*arrow*). A Nabothian cyst is seen in the cervical stroma (*arrowhead*). **B** Dynamic MR images (200/26; upper left, precontrast; upper right, early phase; lower left, late phase 1; lower right, late phase 2) show early enhancement of the tumor (*arrow*). A hyperintense rim is visible (*arrowheads*). The enhanced region extends to the Nabothian cyst and the posterior margin of the cervical stroma. **C** Macroscopic section (hematoxylin–eosin) of the posterior lip of the uterine cervix. The depth of tumor (*arrow*) invasion is less than one-third of the cervical stroma. The Nabothian cyst (*arrowhead*) is separate from the tumor. The *large arrow* indicates the posterior vaginal wall.

Fig. 2. Cervical squamous cell carcinoma in a 32-year-old woman. **A** Parasagittal T2-weighted MR image shows a high-intensity lesion (*arrows*) in the whole stroma; no residual stroma is seen. **B** In all dynamic phases (upper left, precontrast; upper right, early phase; lower left, late phase 1; lower right, late phase 2), a hyperintensely enhanced lesion is seen in the whole stroma (*arrow*). Ringlike enhancement is seen in the peripheral portion of the tumor (*arrowheads*). **C** Microscopic image (hematoxylin–eosin, ×40) shows the tumor (*arrow*) and residual stroma without tumor invasion. In the stroma, massive edema (*large arrow*) and peritumoral inflammatory cell infiltration (*arrowheads*) are visible.

Table 1. Histopathological and MR findings correlation for the uterine cervical cancer stromal invasion

Number of cases	Histopathology	T2WI[a]	Dynamic images		Postcontrast T1WI[b]	Surgical FIGO classification
			Early phase	Late phase		
5	Partial	Partial	Partial	Partial	Partial	Ib
2	Partial[c]	Partial	Partial	Complete	Complete	Ib
3	Partial	Partial	Complete	Complete	Complete	Ib (N = 2), IIa (N = 1)
5	Partial[d]	Complete	Complete	Complete	Complete	Ib
3	Complete	Complete	Complete	Complete	Complete	Ib (N = 1), IIb (N = 2)
2	Complete	Complete	Complete	Unevaluable	Unevaluable	IIa (N = 1), IIb (N = 1)

[a] T1WI = T1-weighted images
[b] T2WI = T2-weighted images
[c] One case accompanying an inflammatory lesion in the peritumoral cervical stroma
[d] One case accompanying an inflammatory lesion and a massive edema in the peritumoral cervical stroma

Materials and Methods

Patients

Twenty-five consecutive patients with untreated primary cervical cancer of the uterus underwent MR studies before surgery. Five patients were excluded from the study because of the invisibility of microscopic tumors and the poor image quality. The MR images of the remaining 20 cases were evaluated (mean age = 49.3 years; range = 30–69 years). Radical hysterectomy was performed in all 20 patients. Bilateral oophorectomy was performed in 10 patients older than 50 years. The surgical/pathological stage was determined according to the classification of the International Federation of Gynecological and Obstetrics (FIGO): Ib in 15 cases, IIa in two cases, and IIb in three cases. The histologic types were squamous cell carcinoma (14 cases), adenocarcinoma (four cases), and adenosquamous carcinoma (two cases).

MR Imaging Techniques

MR imaging was performed with a 1.5-T superconducting magnet (Magnetom; Siemens; Erlangen, Germany). T2-weighted SE images were obtained in the transverse and sagittal planes with 1800/70 (repetition time in ms/echo time in ms) and two acquisitions. After T2-weighted SE images, dynamic study was performed in the sagittal plane. A gadopentetate dimeglumine (Gd-DTPA, Magnevist; Nihon Schering; Osaka, Japan) was hand injected at 0.1 mmol/kg. Three sections of dynamic imaging were obtained with 200/15–26, one acquisition, and scanning time of 40 s at the center of tumor. Dynamic MR images were obtained before, just after (early phase), 1 min after (late phase 1), and 2 min after (late phase 2) contrast material administration. After the dynamic study, postcontrast T1-weighted SE images (600/15–26) were obtained in the sagittal plane. The matrix was 256 × 192, with a 27.8-cm field of view, and the section thickness was 5 mm, with an intersection gap of 0.5 mm in each sequence.

Analysis of Diagnostic Accuracy of MRI for Stromal Invasion by Cervical Carcinoma and the Reasons for Misdiagnosis

Sagittal plane of T2-weighted SE images, dynamic images, and postcontrast T1-weighted images in the 20 patients were read blindly by two radiologists (K.T. and T.M.). They had no knowledge of the histological depth of stromal invasion by cervical cancer. Each pulse sequence was assessed independently. Interpretation discrepancies were resolved by consensus.

The cervical cancer was depicted as a high-intensity tumor on the T2-weighted SE images and as an enhanced region on the dynamic and postcontrast T1-weighted images. The depth of stromal invasion on the T2-weighted and on the dynamic and postcontrast T1-weighted images was evaluated according to the previously reported criteria [1, 3, 4, 7–9]. The degree of invasion was classified as partial stromal invasion or complete stromal invasion.

Occasional presence of a hyperintensely enhanced rim around a tumor has been reported on dynamic and postcontrast T1-weighted images [7, 8]. This rim has been reported to be helpful in evaluating the extent of stromal invasion by the tumor [7]. The presence of a ring-enhanced area around the tumor was also independently evaluated on the dynamic and postcontrast T1-weighted images. In evaluating the degree of stromal invasion, a hyperintense rim was regarded as a tumor.

Histological Correlation

Histological specimens prepared in the same sagittal plane as the MR images were directly compared with sagittal MR images. We evaluated the diagnostic accuracy of each sequence for stromal invasion and used the McNemar test for statistical analysis. In addition, we tried to identify the pathological changes responsible for misdiagnosis. The pathologist (H.O.), without knowledge of the imaging findings, used hematoxylin and eosin staining to examine these specimens, paying special attention to the tumor extension, inflammatory cell infiltration, and edema in the tumor and the stroma. The hyperintense rim region was also correlated with the histological changes.

Results

Table 1 summarizes the results of evaluation of the tumor invasion into the cervical stroma on sagittal MR images, with correlation with the histopathological evaluation. Histologically, the tumor partially invaded the cervical stroma in 15 patients and totally invaded the stroma in the other five patients in the sagittal direction. There were no cases with extrauterine invasion in the sagittal plane (invasion to the bladder or rectum).

Among the 15 cases with partial invasion, the degree of stromal invasion was correctly diagnosed on the T2-weighted images in 10 patients, early-phase dynamic images in seven patients, and late-phase dynamic images and postcontrast T1-weighted images in five pa-

tients (Table 1, Fig. 1). In the cases of misdiagnosis, the tumor was diagnosed as a complete stromal invasion (Fig. 2). Among the five patients with complete stromal invasion, the depth of invasion was correctly diagnosed on T2-weighted images and early-phase dynamic images in all five patients and on late-phase dynamic images and postcontrast T1-weighted images in three patients (Fig. 3). In the two misdiagnosed cases, it was impossible to identify the tumor on late-phase dynamic and postcontrast T1-weighted images because the signal of the tumor was isointense relative to the surrounding tissue.

As a total, correct diagnosis of the tumor extension into the cervical stroma was achieved in 15 of the 20 patients on T2-weighted images, in 12 patients on early-phase dynamic images, and in eight patients on late-phase dynamic and postcontrast T1-weighted images. The diagnostic accuracy of T2-weighted imaging was significantly different from that of postcontrast T1-weighted imaging (McNemar test; $p < 0.05$). The difference of other pairs was not significant. The 95% confidence intervals of the difference in the diagnostic accuracy were $-0.05-0.36$ for T2-weighted imaging versus dynamic imaging, $-0.25-0.42$ for dynamic imaging versus postcontrast T1-weighted imaging, and $0.09-0.61$ for T2-weighted imaging versus postcontrast T1-weighted imaging.

We evaluated the peritumoral stroma histologically because overestimation of the tumor extension is due to abnormal intensity or abnormal enhancement of cervical stroma. In one of two patients overestimated only on late-phase dynamic and postcontrast T1-weighted images, peritumoral inflammatory cell infiltration (0.5 mm in width) was observed (Table 1). In one of the five patients overestimated on all images, massive edema and inflammatory cell infiltration (0.5 mm in width) were observed in the peritumoral stroma (Table 1, Fig. 2). However, these peritumoral pathological changes (inflammation or edema) were not found in the other overestimated patients. In five cases with complete stromal invasion, pathological examination of the residual cervical stroma was impossible because there was no remaining stromal tissue.

In five of the 20 patients examined, a ring-shaped hyperintense rim was observed on dynamic images (Figs. 1–3). In four of those five cases, the hyperintense rim could not be clearly identified on postcontrast T1-weighted images because the signal intensity of the rim was similar to that of the stroma and myometrium. Tumor invasion was partial in two of the five patients, and the whole cervical stroma was involved in the other three. Histologically, of the two patients with partial stromal invasion, the rim region corresponded with peritumoral massive edema in one patient and with the normal stroma without inflammation in the another patient. In the other three patients with a hyperintense rim, the tumor invaded the whole stroma, and histologically the

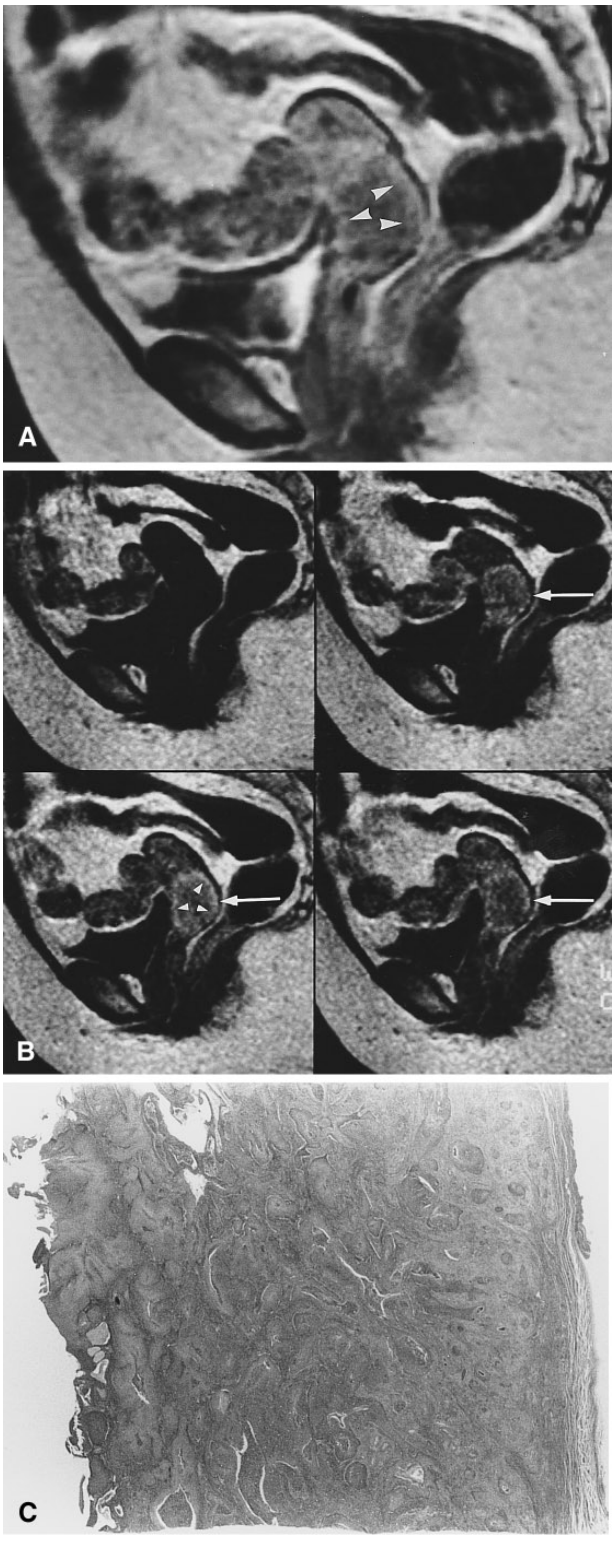

Fig. 3. Cervical squamous cell carcinoma in a 68-year-old woman. **A** Postcontrast T1-weighted image shows the rim (*arrowheads*) less prominently. **B** Dynamic MR images (upper left, precontrast; upper right, early phase; lower left, late phase 1; lower right, late phase 2) show a tumor (*arrow*) extending into the whole stromal layer, with a hyperintense rim (*arrowheads*) in all postcontrast phases. **C** Microscopic section (hematoxylin–eosin, ×40) shows the tumor extending into the whole stroma.

rim corresponded with the periphery of the tumor and not with an inflammatory region.

Discussion

Several studies have shown that T2-weighted imaging is most useful for determining the extent of cervical cancer invasion [1–6]. Postcontrast T1-weighted images were reported to be inferior to T2-weighted images [8, 9]. Our present study confirmed this. A prior report [7] described early-phase images of dynamic MRI as showing good contrast-to-noise ratio and that the diagnostic accuracy with dynamic images was superior to that with T2-weighted images. However, in this study the accuracy of T2-weighted images was higher than that of the dynamic images.

Our results suggest that overestimation of the tumor extension is due mainly to abnormal high intensity of the histologically normal cervical stroma on T2-weighted images or on enhanced images. It remains unknown why the normal cervical stroma shows abnormal high intensity. It may be related to increased vascularity in the peritumoral stroma, which we could not detect on hematoxylin-and-eosin-stained sections: specific immunohistochemical staining for the capillary vessels (CD-31 or vimentin staining) may be needed.

Overestimation was more common with dynamic images than with T2-weighted images in this study. Our results were inconsistent with those in the previous report [7]. The discrepancy might be explained as follows: because the peritumoral cervical stroma was abnormally enhanced more frequently in the late-phase dynamic study, early-phase dynamic images may be better for diagnosing tumor extension. Although the scanning time per session of the dynamic study was about 40 s in this study, a shorter scanning time (25.6 s) was employed, and this difference in scanning time may be a reason for the inconsistent results.

A hyperintense rim around cervical tumors is often found on dynamic MR images [7] and seldom on postcontrast T1-weighted images [8]. The incidence of this finding is variable: two out of 31 cases (6%) according to Hricak et al. [8] and eight out of 18 cases (44%) according to Yamashita et al. [7]. In this study, we observed a rim in five of the 20 patients (25%) on dynamic images but in only one patient (5%) on postcontrast T1-weighted images. The low incidence on the postcontrast T1-weighted images was due to a less-prominent hyperintense rim because of similar enhancement of both the surrounding stroma and the myometrium.

Although a hyperintense rim corresponding with reactive inflammation around the tumor and useful for the evaluation of the extent of tumor invasion has been reported [7], we failed to obtain a consistent result. That is, histologically, a hyperintense rim corresponded with the periphery of the tumor itself in three patients, peritumoral edema in one patient, and the normal stroma in one patient. Our results indicate that a hyperintense rim around a cervical tumor is not useful for determining the degree of stromal invasion by the tumor and may be one cause of misdiagnosis.

Our results suggest that T2-weighted imaging is the most useful sequence for evaluating the degree of stromal invasion by uterine cervical cancer and that misdiagnosis occurs more frequently with dynamic and postcontrast T1-weighted images than with T2-weighted images. Overestimation arises mainly from abnormal intensity of the normal cervical stroma. A hyperintense rim corresponds to either the tumor, edema, or the intact stroma. This rim does not seem to be useful for determining the tumor extension and may be one cause of misdiagnosis.

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