



# Soft Tissue Metastasis in Patients with Primary Malignancies; Magnetic Resonance Imaging and Clinical Evaluations

원발암이 있는 환자에서 연조직 전이; 자기공명영상과 임상적 평가

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**Purpose:** The purpose of this study was to evaluate the clinical and magnetic resonance imaging (MRI) findings of soft tissue metastases distinct from benign soft tissue lesions.

**Materials and Methods:** We retrospectively analyzed the MRI findings of soft tissue lesions found incidentally in patients with primary carcinoma and those without primary carcinoma from 2002–2015. To evaluate the features of soft tissue metastases distinct from benign soft tissue lesions, patients with benign soft tissue lesions were randomly selected and statistically analyzed for the distinctive features of the two groups.

**Results:** A total of 47 patients (mean age 46.2 years) and 36 controls (mean age 46.2 years) were enrolled. Thirty six of the 47 patients were diagnosed with soft tissue metastasis, most commonly as the primary cancer (31%). The most common site of soft tissue metastasis was the lower extremities (36%) followed by the upper extremities (31%). Soft tissue metastasis was statistically significantly different from benign soft tissue lesions according to patient age, lesion size, margin, presence of degenerative changes in lesions, and presence of edema around the mass.

**Conclusion:** If the incident soft tissue lesion shows malignant features on MRI in patients with primary carcinoma or in patients over 40 years of age, the radiologist should consider the possibility of metastatic cancer.

## Index terms

Soft Tissue Neoplasms  
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## INTRODUCTION

Metastatic tumors presenting as soft tissue masses are relatively rare compared to bony metastasis or direct invasion by carcinoma (1-3). They are usually misdiagnosed as a soft tissue sarcoma on imaging studies, and can be the source of diagnostic confusion both clinically and pathologically. The distinction between a soft tissue metastasis and primary soft tissue tumor or inflammation is important, because the treatment and prognosis are significantly different (1, 4, 5). Moreover, the metastatic tumors to soft tissue are known to have poor prognosis (1, 6).

However, in most cases, the distinction between a primary soft tissue sarcoma and metastatic carcinoma is difficult without biopsy (6).

Although there have been several case reports of skeletal muscle metastases from lung, breast, colonic, renal, ovarian, gastric, esophagus, melanoma, and sarcoma (3, 5, 7-12), imaging findings of soft tissue metastases, including magnetic resonance imaging (MRI) and computed tomography (CT) appearance are usually non-specific (13). Also, to our knowledge, there are few original reports about the features of MRI for soft tissue metastasis involving muscle or subcutaneous fat layer.

In this study, we evaluated clinical data and MRI findings of soft tissue metastases distinct from benign soft tissue lesions.

## MATERIALS AND METHODS

### Patients

This study was approved by our Institutional Review Board (No. E-2017011), and informed consent was waived due to retrospective study.

We retrospectively evaluated the soft tissue lesions incidentally found in patients with a primary malignancy between 2002 and 2015. Initially, we obtained a list of patients with pathologically proven metastases to the muscle or subcutaneous fat layer during the same period from the pathology department. We searched the patients with soft tissue tumor who already have known primary cancer in our radiologic report searching system. We combined the data and excluded patients who do not undergo MRI for the soft tissue lesions. Lesions without pathologic confirmation were excluded. Also, cases that represented metastases to lymph nodes and with soft tissue involvements of lymphoma or leukemia were excluded. Finally, 47 patients (25 females, 22 males; age range 36–89 years, mean age 60.7 years) were enrolled. For comparison with soft tissue metastases, 36 patients (19 females, 17 males; age range 7–82 years, mean age 46.2 years) with pathologically proven benign soft tissue tumors within the same period were selected through an imaging readout database and these patients were classified as control group.

Clinical data investigated included patient age, gender, pathologic type of primary cancer, clinical symptoms at the time of soft tissue lesion discovery (initial presenting symptoms), period between diagnosis of primary cancer and detection of soft tissue lesions, and histologic findings of incidentally detected soft tissue lesions.

Distant metastasis to other sites, such as bone or solid organs, was investigated based on the patient's clinical records and images of other departments, including bone scan or positron emission tomography (PET)-CT, or images of other areas, such as abdomen or chest CT scans.

### Image Analysis

Two radiologists with 4 and 12 years experience in musculoskeletal imaging, respectively, retrospectively reviewed the MRI

scans using a picture archiving and communication system. Decisions were reached by discussion and consensus.

Conventional MRI data contained T1- and T2-weighted fast spin-echo sequences with/without fat-suppression using essentially axial planes and alternative sagittal or coronal planes. Delayed enhanced images were also obtained in three planes by fatsuppressed, fast spin-echo T1-weighted imaging.

Evaluations of the MRI scans included number of lesions, lesion size, margins, locations (anatomical location and depth of the lesion), lesion homogeneity, presence of soft tissue edema around the lesion, presence of degenerative changes within the lesion, and presence of cortical erosion or bony involvement by expansion or infiltration of soft tissue lesion.

We defined multiple lesions as having more than one soft tissue lesion within the scan range. The size of the lesion was defined as the longest diameter by measuring the long axis. In a patient with multiple lesions, the largest lesion was analyzed. The margin of a lesion was simply classified as well- or ill-defined. Well-defined margin was defined as the case where the entire lesion was clearly bounded to the surrounding normal structures and ill-defined margin was defined as a case where some or all the lesion was unclear or ambiguous to the surrounding normal structure. The locations of a lesion were basically investigated based on anatomical locations and classified as deep (deep to compartmental fascia) or superficial (involving skin and subcutaneous fat).

The homogeneity of the lesion was simply classified as homogeneous and heterogeneous, and assessed on both T1 weighted images (T1WIs) and T2 weighted images (T2WIs). The soft tissue edema was defined as the appearance of infiltrative high signal intensity around the lesion on T2WI and contrast-enhanced image. The degenerative change within the lesion was defined as a lesion with high signal intensity on T2WIs that was not enhanced on the contrast-enhanced image or high signal intensities on T1WIs and T2WIs representing hemorrhage. Degenerative changes included cystic necrosis and hemorrhage.

### Statistical Analyses

Fisher's exact test and Mann-Whitney U test were used to determine whether gender, patient symptoms, lesion location (deep or superficial), and margin, lesion homogeneity, presence of soft tissue edema around the lesion, degenerative change with-

in the lesion, and presence of cortical erosion or bony involvement may affect the distinction between soft tissue metastases and benign soft tissue lesions. For age and lesion size, we used two-sample t-test. The analysis was performed using SPSS statistics version 21 (IBM Corp., Armonk, NY, USA). Statistical significance was accepted for  $p < 0.05$ .

## RESULTS

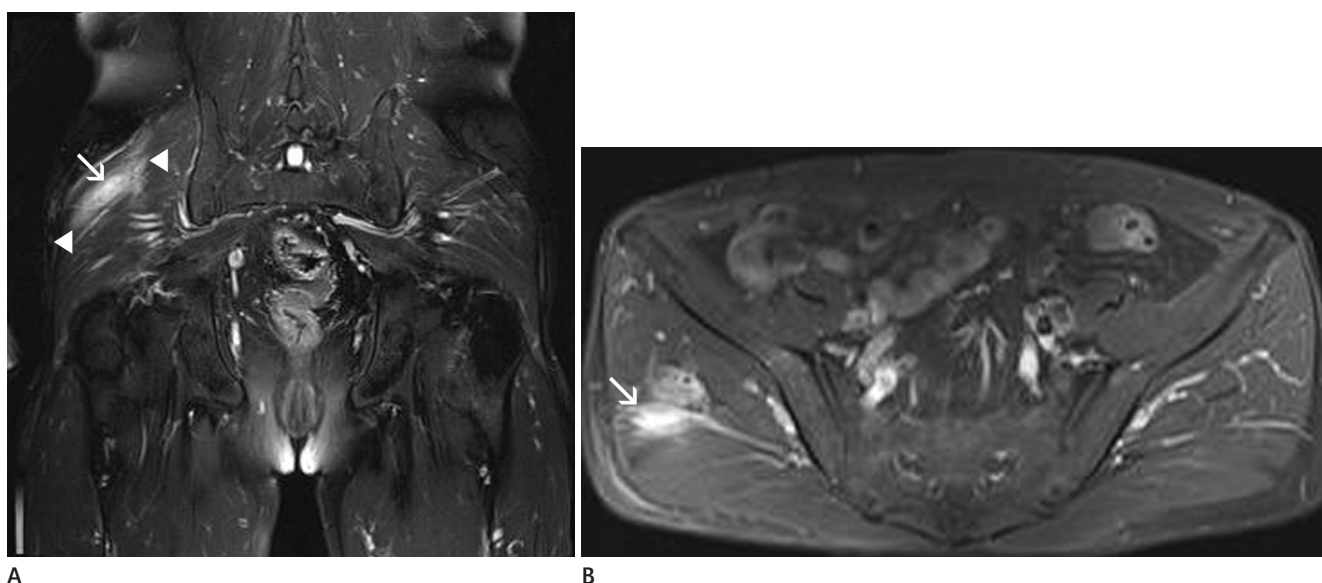
Thirty-six (15 females, 21 males, mean age 63 years, age range 36–89 years) of 47 patients (77%) were diagnosed with soft tissue metastases. Ten patients (9 females, 1 male, mean age 53 years, age range 40–72 years) had benign soft tissue lesions. In the remaining patient with thyroid cancer, the soft tissue lesion was diagnosed as myxofibrosarcoma. Thirty-three patients had a single soft tissue lesion (Fig. 1) and the remaining 14 had multiple lesions (Fig. 2). Of the 36 patients with soft tissue metastases, 14 had multiple lesions and 12 had a single lesion. Of the 10 patients with benign soft tissue lesions, only one patient with hemangiomas had multiple lesions. All patients in the control group had a single mass. On the other hand, in 17 of 47 patients, soft tissue lesions were found incidentally without knowledge of the presence of primary cancer (Fig. 3). Among those 17 patients, we interpreted primary malignant tumors in 9 patients

with single soft tissue lesion and metastases in 8 patients with multiple soft tissue lesions in the first MRI scans. The benign soft tissue tumors of control group included schwannoma ( $n = 13$ ), hemangioma ( $n = 6$ ), benign lipomatous tumor ( $n = 4$ ), giant cell tumor ( $n = 3$ ), nodular fasciitis ( $n = 3$ ), glomus tumor ( $n = 2$ ), epidermal cyst ( $n = 2$ ), leiomyoma ( $n = 1$ ), myxoma ( $n = 1$ ), and pilomatricoma ( $n = 1$ ).

The types of primary malignancies and the number of patients diagnosed with soft tissue metastasis according to each primary malignancy are summarized in Table 1. Among all primary tumors, lung cancer was the most common (26%) and the majority of soft tissue metastasis originated from lung cancer (31%). The pathologic results of three unknown primary origin were poorly differentiated squamous cell carcinoma, melanoma, and primitive neuroectodermal tumor (PNET).

The anatomical locations of soft tissue lesions are summarized in Table 2. Metastatic soft tissue lesions ( $n = 36$ ) were the most common in the lower extremities (thigh, lower leg, ankle, and toe; 13/36, 36%), followed by the shoulder (6/36, 17%) and the upper extremities (upperarm, forearm, finger, hand, and wrist; 5/36, 14%).

Among 36 patients with soft tissue metastases, 11 complained of pain. In the control group, 14 patients had pain. The symptom was not significant for differentiating between metastatic and



**Fig. 1.** A 50-year-old male patient diagnosed with oropharyngeal cancer two years previously and presently complaining of buttock pain. **A.** On coronal fat-suppressed T2-weighted image of the pelvis, a hyperintense soft tissue lesion with ill-defined margin (arrow) is seen in the muscular layer of the right buttock. Peritumoral edema (arrowheads) is also noted. **B.** The lesion shows homogeneous enhancement without degenerative change within the lesion (arrow) on axial fat-suppressed, contrast-enhanced T1-weighted image.

benign lesions ( $p > 0.05$ ).

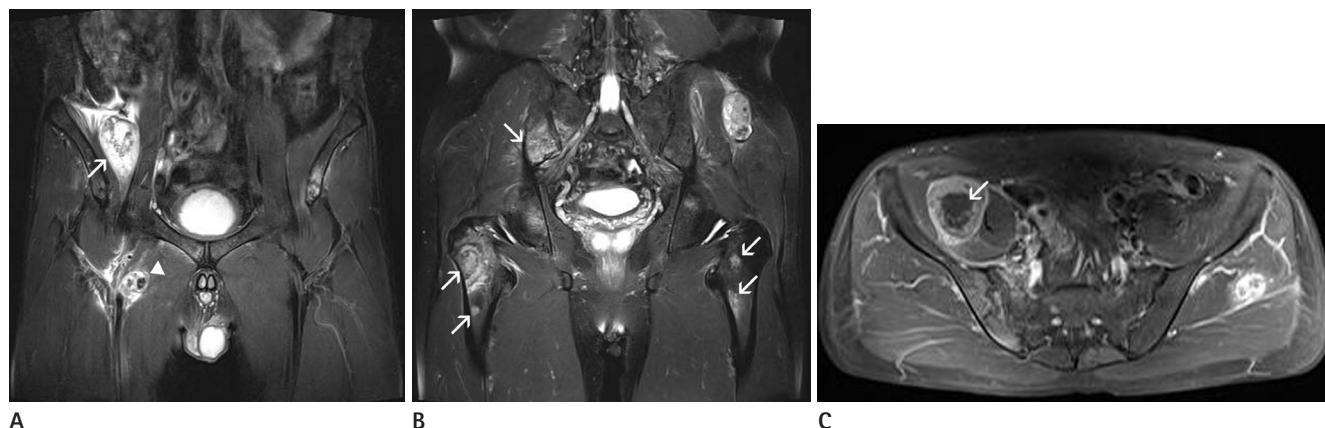
Thirteen of 36 patients (36%) diagnosed with soft tissue metastasis had distant metastasis to bone or other solid organs (Fig. 2).

Results of statistical analyses to differentiate between soft tissue metastasis and benign soft tissue lesion are summarized in Table 3. Age, lesion size, margin, degenerative change within

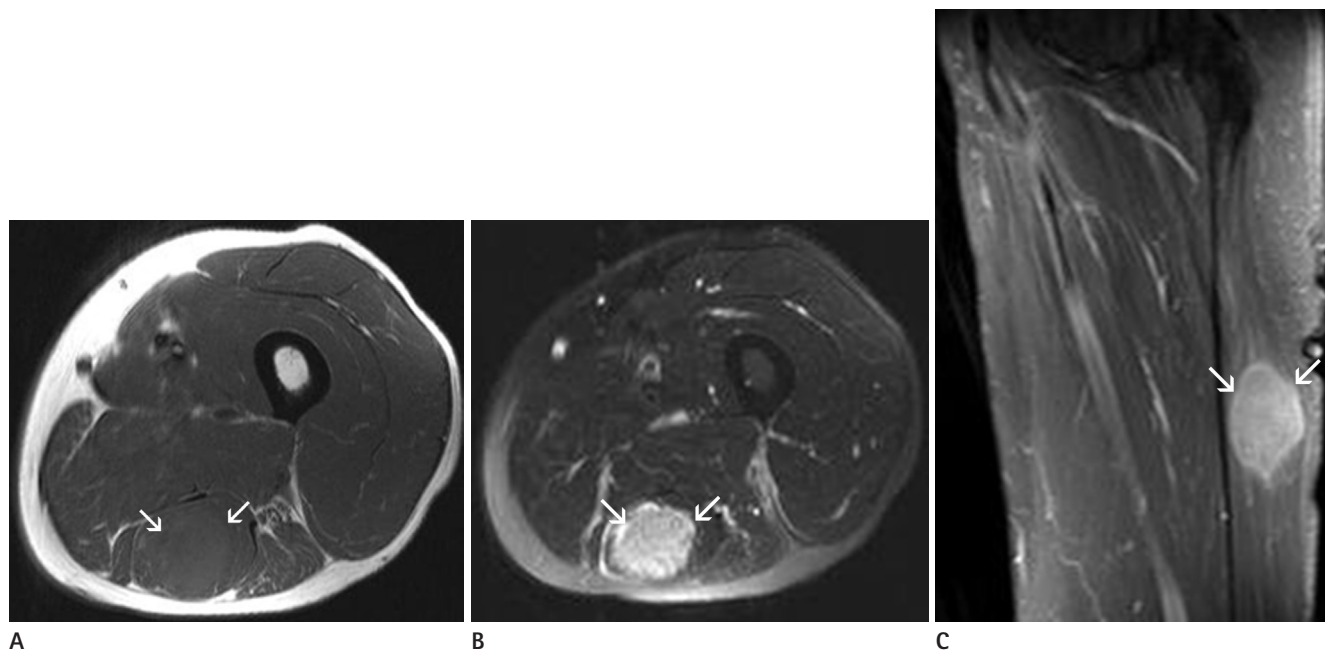
the mass, and the presence of edema around soft tissue lesions (Fig. 1) were statistically significant.

## DISCUSSION

Distant metastases to soft tissue are relatively uncommon, even



**Fig. 2.** A 47-year-old male patient with multiple bone and soft tissue lesions. After biopsy for soft tissue lesion, lung cancer was diagnosed.  
**A.** On coronal fat-suppressed T2-weighted image of pelvis, two heterogeneous soft tissue masses with peritumoral edema are seen within each iliopsoas (arrow) and adductor muscle (arrowhead).  
**B.** On another scan of same sequence, multiple bone metastatic lesions are seen (arrows).  
**C.** Metastatic mass located within the right iliopsoas muscle shows degenerative change (arrow) on axial fat-suppressed contrast enhanced T1-weighted image.



**Fig. 3.** A 67-year-old male patient with intramuscular metastasis and unknown lung cancer.  
**A.** On axial T1-weighted magnetic resonance image of left thigh, a homogeneous mass lesion (arrows) is seen in the semitendinosus muscle.  
**B.** The soft tissue lesion (arrows) shows well-defined margin without peritumoral edema on axial fat-suppressed T2-weighted image.  
**C.** On sagittal fat-suppressed, contrast-enhanced T1-weighted image, the mass lesion (arrows) shows homogeneous enhancement without degenerative change.

in patients with known cancers and despite comprising approximately 55% of our body mass (2, 14). Some previous studies reported a relatively broad range of frequency, and these frequency differences might be considered to depend on the procedures used for the examinations or active examinations or autopsy cases (1, 3, 4). Several factors may contribute to the rarity of hematogenous metastases to soft tissue areas. For example, organs with a high incidence for metastatic carcinomas, such as the liver, lung, or bone, are rich in capillary vasculature and have a constant blood flow, whereas in soft tissues, such as skeletal

muscle, the blood flow is variable and subject to variations in tissue pressure affecting tumor implantation (6, 8, 14, 15). Also, some authors suggested that lactic acid production by muscle inhibits growth of tumor studies, and uncommon hematogenous metastases to muscles are thought to be due to muscle motion, muscle pH, and the muscle's ability to remove tumor-produced lactic acid (11, 14, 16, 17). Leukemia and lymphoma are the most frequent cancer of metastases to muscle (11).

With regard to the primary malignant tumor, several studies (1, 6, 13, 18, 19) reported that the most frequent tumor of origin was lung cancer, similar to our series. However, many other studies reported different tendencies for the common source causing soft tissue metastases (1, 2, 13), and a variety of malignant

**Table 1. The Types of Primary Malignancies and the Number of Patients Diagnosed with Soft Tissue Metastasis According to Each Primary Malignancy**

Primary Malignancy	Number of Patients	Soft Tissue Metastasis
Lung cancer	12	11
Breast cancer	6	2
Thyroid cancer	5	2
Colorectal cancer	5	5
Stomach cancer	2	2
Hepatocellular cell carcinoma	2	2
Oropharyngeal cancer	2	0
Melanoma	2	2
Cholangiocarcinoma	2	2
Bowen's disease (Squamous cell cancer <i>in situ</i> )	1	1
Hemangiopericytoma	1	1
Renal cell carcinoma	1	1
Gall bladder cancer	1	1
Uterine cervical cancer	1	1
Plasmacytoma (multiple myeloma)	1	0
Unknown origin	3	3
Total	47	36

**Table 2. The Anatomical Locations of Soft Tissue Lesions**

Locations	Metastasis	Control Group
Neck area	0	3
Shoulder	6	0
Upperarm	2	5
Elbow	1	0
Forearm	1	1
Finger/hand/wrist	1	6
Pelvic area	4	3
Thigh	7	4
Lower leg	6	5
Ankle	0	1
Toe	0	2
Back area (muscle & subcutaneous fat)	1	4
Psoas muscle	3	2
Chest wall	3	0
Abdominal wall	1	0
Total	36	36

The location of one new malignant tumor (myxofibrosarcoma) was thigh.

**Table 3. Clinical and Magnetic Resonance Imaging Analysis Results for Differentiating between Soft Tissue Metastasis and Benign Soft Tissue Lesion**

	Soft Tissue Metastasis	Benign Lesion	p-Value
Age (years)	62.83 ± 2.45	46.22 ± 3.05	< 0.0001
Gender (M:F)	21:15	17:19	0.348
Size (cm)	7.5 (2.8–26)	3.5 (0.4–11.6)	0.001
Symptom	n = 11	n = 14	0.461
Location (deep: superficial)	30:6	25:11	0.168
Margin (well:ill)	10:26	32:4	< 0.0001
Homogeneity	16	11	0.227
Degenerative change within the mass	16	8	0.047
Bone erosion	6	5	0.745
Peritumoral edema	28	8	< 0.0001
Mineralization	2	2	1



tumors including skin cancer, renal cell carcinoma, melanoma, breast cancer, and colon cancer can cause soft tissue metastases (13, 20-23). In our study, the most common tumors metastasizing to soft tissue were carcinomas of the lung and colon. In one study (2), malignant melanoma was the most frequently specific tumor type that metastasized to soft tissue. However, there were only two cases of melanoma metastasis to soft tissue in our study.

Many metastatic tumors to soft tissue present as occult metastases from an unrecognized primary (2, 7, 24). Also, in this study, 17 soft tissue metastatic lesions were found incidentally without knowledge of the presence of primary cancer. Among the 17 incidental metastases, 9 had solitary soft tissue metastasis. Because the imaging characteristics of these lesions are nonspecific and there is considerable overlap in the appearance of metastatic lesions and primary soft tissue sarcomas, the diagnosis of solitary soft tissue metastasis in patients with unknown primary malignancy is very difficult. On MRI, large, multinodular, and hypervascular soft-tissue sarcomas may have central areas of hemorrhage, necrosis, and calcification (25). However, hemorrhage may occur within a primary or metastatic soft-tissue tumor. Also, peri-lesional edema may occur in soft tissue sarcoma, metastasis and infection.

The frequent metastatic site varies (1, 2, 13), with the thigh muscles, iliopsoas, and paraspinal muscles reported as common sites (3, 6, 20, 21, 26). In this study, the most frequent site of metastasis to soft tissue area was the lower extremity, followed by the shoulder. These results contrast with previous studies (1, 2, 11, 13). These differences might be caused by the composition of the primary cancer. In this study, among 36 patients with soft tissue metastasis, 11 patients had lung cancer. In these patients the lesions were located in a lower leg ( $n = 4$ ), shoulder ( $n = 3$ ), thigh ( $n = 2$ ), pelvic area ( $n = 1$ ), and psoas muscles ( $n = 1$ ). Given the ease of arterial metastasis of lung cancer, lesions can easily metastasize to distal extremities. In our study, the proportion of the lung cancer in primary malignancies was high, which might affect the anatomical site of the soft tissue metastasis. The anatomic distribution of metastases to soft tissue area in this study was similar to the distribution of soft tissue sarcoma, with 36% occurring in the lower extremity. Thus, metastatic carcinoma can often be confused clinically and histologically with primary soft tissue sarcoma. Soft tissue metastases can occur in

muscles and subcutaneous sites, but the incidence of subcutaneous fat involvement has been reported to be lower than that of muscle involvement. It is believed that subcutaneous metastases might be underreported in the literature (13).

Several authors (13, 27) suggested that soft tissue metastases, especially those in skeletal muscle, are frequently painful or palpable, and a painful soft tissue mass is more commonly noted in patients with soft tissue metastasis than in primary sarcoma (19). In this study, 20 of 36 patients (56%) with soft tissue metastases complained of pain or palpable mass. However, the presence of symptom was not significant, and we could not compare symptoms between sarcoma and soft tissue metastases because our study did not include sarcomas. Clinical presentation, anatomic distribution, and radiographic imaging studies of metastases to soft tissue area are similar to those of soft tissue sarcomas (6). Because the treatment and prognosis are different, differentiating between these diseases is important, but difficult (3, 6). Moreover, the metastases of carcinomas to soft tissue appears to be a late event in the progression of the disease and the overall prognosis is poor (2, 6, 18). However, distant metastases to other sites occurred only in 36% of our cases.

MRI has become the preferred technique for distinguishing soft tissue metastases from other tumorous processes (28). In several previous studies (11, 13, 19, 24, 29), MRI revealed soft tissue metastases to have poorly defined margins, large areas of central necrosis, and extensive peritumoral edema, but rare erosion of the adjacent bone. As noted presently, to compare the benign soft tissue lesions and soft tissue metastasis, an ill-defined margin, presence of degenerative change within the lesion, and peritumoral edema are statistically significant findings in soft tissue metastasis.

Soft tissue metastasis was significantly larger than benign soft tissue tumors, and cut-off values were 7.5 cm in diameter. As reported (30), cutaneous metastasis occurs as multiple, small skin nodules. Presently, the proportion of deep locations was high (30/36) and the size of the lesion was large. If the lesions locate deep in the skin layer, the size of the lesion may help to differentiate the benign and malignant tumors. In the same context, as the lesion becomes larger the prevalence of degenerative change within the lesion may increase. Thus, this finding suggests the presence of metastatic lesions than benign soft tissue tumors in patients with known malignancy. Ill-defined margin

with peritumoral edema were the significant findings to differentiate the benign and soft tissue metastasis in this study, but it is present in other benign conditions including infection or inflammatory lesions. So, clinical and radiological findings to exclude the possibility of infection or inflammation may be important. The statistically significant imaging findings in this study were somewhat similar to malignant soft tissue tumors, such as sarcoma or other primary soft tissue malignancies. Therefore, MRI findings of soft tissue metastases are not pathognomonic, and thus, needle or excisional biopsy is mandatory for diagnosis (1, 11, 19, 30). However, MRI evaluation of soft tissue metastases is advisable before biopsy (13). Also, confirmation of past history is important for the early diagnosis (1). Moreover, the diagnosis of soft tissue metastasis should be considered in the differential diagnosis of any painful soft tissue mass with extensive peritumoral enhancement pattern in MRI that would otherwise be most suggestive of a soft tissue sarcoma (13, 19).

There were some limitations in this study. First was the small number of patients. This reflects the low incidence of soft tissue metastasis and exclusion of cases that represented metastases to lymph nodes. We included only cases involving skeletal muscles and subcutaneous fat layers. Second, we could not prospectively perform the recent functional MRI for a more advanced imaging analysis because this study was retrospectively analyzed. However, even functional MRI might be difficult to differentiate between soft tissue metastasis and primary sarcoma because these will show similar malignant imaging findings.

In summary, there were no specific imaging findings to diagnose soft tissue metastasis in this study. Although there were some significant imaging findings differentiating between the benign soft tissue tumors and soft tissue metastasis, these findings were almost the same as in the malignant soft tissue tumors reported in previous studies. Therefore, it is difficult to distinguish between soft tissue metastases and primary malignant tumors. Patients included in our study were all over 40 years of age, except two. When a patient 40 years or older shows nonspecific imaging findings, especially aggressive findings in the bones, radiologists often prefer bone metastasis due to its frequency. On the contrary, because of the rarity of the soft tissue metastasis, we often misdiagnose these diseases. Therefore, in the same context, in patients over age 40 years of age with primary malignancies or who are unaware of the primary malignancies, when there

is non-specific soft-tissue lesion with malignant features are seen on MRI, the possibility of metastasis should be considered, as in the case of bone metastasis, rather than primary malignant tumors. Also, radiologists should try to make a definitive diagnosis through biopsy or special imaging methods such as functional MRI before treatments.

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## 원발암이 있는 환자에서 연조직 전이; 자기공명영상과 임상적 평가적 평가

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**목적:** 본 연구는 양성 연조직 병변과 구분되는 연조직 전이의 임상 소견과 자기공명영상 소견을 찾고자 한다.

**대상과 방법:** 2002~2015년 동안 원발암이 있는 환자 및 원발암을 모르고 있던 환자에서 우연히 발견된 연조직 병변의 자기공명영상소견을 후향적으로 분석하였다. 양성 연조직 병변과 구분되는 연조직 전이의 특징을 평가하기 위해 같은 기간 내 진단된 양성 연조직 병변 대조군을 무작위로 선정하였고, 두 군의 구별되는 특징에 대해 통계학적으로 분석하였다.

**결과:** 총 47명(평균연령 60.7세)의 환자와 대조군 36명(평균연령 46.2세)을 본 연구에 포함하였다. 47명 중에 36명이 연조직 전이로 진단되었다. 전체 연조직 전이 중 원발암이 폐암인 경우가 가장 많았다(31%). 연조직 전이의 가장 흔한 위치는 하지(36%)였으며, 다음으로는 상지(31%)였다. 연조직 전이는 나이, 병변의 크기, 경계, 병변 내 퇴행성 변화의 유무, 종괴주위 부종의 유무에서 양성 연조직 병변과 통계학적으로 유의한 차이를 보였다.

**결론:** 원발암이 있거나 혹은 원발암의 존재를 모르고 있는 40세 이상의 환자에서, 우연히 발견된 연조직 병변이 자기공명영상에서 악성의 특징을 보일 때, 영상의학과 의사는 전이암의 가능성을 생각해야 한다.

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