CT and MRI Findings of Malignant Mixed Müllerian Tumor of the Uterus: Irradiation-associated vs Non-associated

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Purpose: The purpose of this study is to present imaging findings of MMMT developed after irradiation and to compare them with those not associated with irradiation.

Materials and Methods: Patients with pathologically-proven MMMT were divided into two groups; group 1, with a history of pelvic irradiation (n = 9), and group 2, without such history (n = 4). With regard to tumor location, size, extent, degree of myometrial invasion, presence of enhancement, and internal texture of a tumor, we analyzed CT (n = 10) and MR imaging (n = 8) findings in each group.

Results: The tumor was larger in group 1 (average 8.7 cm) than in group 2 (average 5.5 cm). In eight patients in group 1, the endometrial cavity was distended, with remarkable fluid retention, and a mass was found in the fundus or body. The junctional zone was disrupted and hemorrhagic or necrotic foci were found within the mass. In all patients in group 2 and in one in group 1, a tumor had replaced the endometrial cavity, without fluid retention.

Conclusion: Imaging findings of irradiation-associated MMMT appeared to be different from those not associated with irradiation. Where there are findings of a distended endometrial cavity filled with fluid and mural mass, one should be alert to the possibility of irradiation-associated MMMT.

Index Words: Uterine neoplasms, CT
Uterine neoplasms, MR

Malignant mixed müllerian tumors (MMMT) are rare uterine malignancies derived from the multipotential cells of müllerian mesenchyme, some are known to occur in elderly postmenopausal women with a history of pelvic irradiation. Though it is uncertain that these tumors are either coincidental malignancies or radiation-induced, the clinicopathologic pattern of radiation-associated MMMT and of MMMT which is not related to irradiation show no points of differentiation (1).

We encountered ten patients with irradiation-associated uterine MMMT, prompting us to evaluate these tumors and to compare them with a group of non-irradiated MMMT. To our knowledge, there has been no report concerning the imaging findings of MMMT developed after pelvic irradiation. Recent reports concerning MR imaging findings of MMMT showed nonspecific results and did not mention a history of previous irradiation (2-4).

We present CT and MR imaging findings of MMMT developed after pelvic irradiation for cervical carcinoma in ten patients. We also compared them with those of MMMT not related with irradiation in five other patients.

Materials and Methods

Between January 1989 and March 1995, we retrospectively reviewed the imaging findings of 15 patients with pathologically documented MMMT. We divided the patients into two groups: group 1, with a
history of irradiation (n = 9) and group 2, without such history (n = 4) (Table 1).

The patients in group 1 were between 43 and 72 years old (mean, 58.2) and in group 2 were between 21 and 81 (mean, 48.5). Their presenting symptoms and signs were vaginal bleeding (two in group 1, four in group 2) followed by abdominal distention and pelvic mass (seven in group 1, none in group 2). All patients in group 1 had a history of previous radiation therapy for squamous cell carcinoma of the cervix, during which the dosage had been 57-75 Gy (mean, 69.7 Gy). In one patient, who had been treated at another hospital, the exact dosage was uncertain. The interval between radiation therapy and the discovery of MMMT ranged from 6 to 17 years (average, 9.5).

Staging was carried out according to the classification of the International Federation of Obstetrics and Gynecology. In group 1, three were classified as stage I, two as stage II, one as stage III, and three as stage IV. Six patients underwent radical hysterectomy, providing pathologic specimens for comparison with imaging findings. The remaining three patients underwent punch biopsy or endometrial curettage, which proved positive. In group 2, three were classified as stage I and one as stage II. For diagnosis, three patients underwent radical hysterectomy and one, endometrial curettage.

Histologically, all patients showed heterologous sarcoma (chondrosarcoma or rhabdomyosarcoma), except one in group 2 who showed homologous sarcoma (leiomyosarcoma). The homologous type was defined as carcinoma plus leiomyosarcoma, stromal sarcoma, fibrosarcoma, or a mixture of these, while the heterologous type was defined as carcinoma plus heterologous sarcoma, with or without homologous sarcoma (3).

In ten patients, CT scans were obtained using a GE CT/T 9800 (General Electric Medical System, Milwaukee, USA) at 10 mm thickness. In eight, MR images were obtained with a 1.0 T unit (SMT-100 X; Shimadzu, Japan). Both T1-weighted [500-700/20-25 (TR/TE)] and T2-weighted [2000-2500/80-95 (TR/TE)] spin-echo images were obtained in sagittal and axial planes. In all patients, enhanced study with gadopentetate dimeglumine (Magnevist, Schering, Germany) was added.

All images were reviewed for location, size, extent, degree of myometrial invasion, presence of enhancement, and internal texture of the tumors. Imaging findings were analyzed by two radiologists (KH Kim, MS Lee) in a blinded fashion to determine any differences in imaging findings between the two groups. They were also blinded as to the stage of the tumor at the time when the findings were analyzed.

### Results

#### Irradiation-associated Group 1

Tumor size was 3-16 cm (average, 8.7 cm) in the greatest dimension.

CT scans revealed a large amount of fluid retention in the endometrial cavity and polypoid endometrial mass effacing the contrast-enhanced myometrial wall (Figs. 1A and 2B). In two patients, hypodense me-

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**Table 1. Summarized Clinical Data of Patients with MMMT**

<table>
<thead>
<tr>
<th>No/ Age</th>
<th>Underlying Disease [carcinoma]</th>
<th>Radiation Dosage (Gy)</th>
<th>Latent Interval (year)</th>
<th>Image Study</th>
<th>Stage</th>
<th>Tumor Size (cm)</th>
<th>Pathology Subtype</th>
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<td>1/49</td>
<td>Cervix IIA</td>
<td>57</td>
<td>7</td>
<td>CT, MR</td>
<td>II</td>
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<td>heterologous</td>
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<td>70</td>
<td>17</td>
<td>CT, MR</td>
<td>II</td>
<td>9</td>
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<tr>
<td>3/54</td>
<td>Cervix IIB</td>
<td>72</td>
<td>8</td>
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<td>III</td>
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<td>12</td>
<td>CT</td>
<td>Ic</td>
<td>3</td>
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</tr>
<tr>
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<td>6</td>
<td>CT</td>
<td>Ib</td>
<td>4</td>
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</tr>
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<td>72</td>
<td>10</td>
<td>CT</td>
<td>IV</td>
<td>10</td>
<td>heterologous</td>
</tr>
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<td>Cervix IIB</td>
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<td>9</td>
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<td>MR</td>
<td>Ib</td>
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<td>heterologous</td>
</tr>
</tbody>
</table>

Note. - OP5 = total hysterectomy and bilateral adnexectomy. RT = radiation therapy. NA = not available.
tastases to the liver and paraaortic lymph node occurred; these were proved by fine needle aspiration under the guidance of sonography and CT.

MR images depicted the tumor. Endometrial fluid retention, cervical or vaginal extension, and myometrial invasion. On T1-weighted images, an endometrial mass showed low or intermediate signal intensity similar to the adjacent pelvic muscles (Fig. 1B, 2C, and 3A). In five patients, intratumoral high signal intensities were seen, suggesting hemorrhagic foci (Fig. 3A). On T2-weighted images, MMMT displayed heterogeneous high signal intensity (Fig. 1D, 2D, and 3B). On the basis of focal loss of junctional zone or irregular interface between the mass and the junctional zone (Fig. 2D), superficial myometrial invasion was demonstrated in two patients, while in three, deep myometrial or serosal invasion was demonstrated (Fig. 1D and 3B). Associated fluid showed high signal intensity on both T1 and T2-weighted images. On enhanced MR images, the masses showed a heterogeneous pattern of strong enhancement (Fig. 1C).

Serial scanning, taken with different imaging features, was used to follow up one patient. Initially a small mass attached to the uterine body was seen; it showed remarkable fluid retention and no obstructing mass extending to the cervix (Fig. 2A). The mass grew rapidly occupying the endometrial cavity and disrupting the junctional zone on MR imaging (Fig. 2C and 2D); hemorrhagic and necrotic foci developed within it. In a later phase, this mass occupied the entire uterus.

**Non-irradiated Group 2**

Tumor size was 4-7 cm (average, 5.5 cm) in the greatest dimension, which was smaller than in group 1. In the endometrial cavity, fluid retention was not demonstrated; in all patients, a solid mass replaced this cavity.

CT scanning showed an enlarged uterus and a hypodense mass within the endometrial cavity with slight peripheral enhancement. MR findings were similar to those of group 1 except for the absence of endometrial fluid retention (Fig. 4). Because of this absence, the mass could not be differentiated on either CT or MR imaging from an endometrial carcinoma or a degenerated submucosal leiomyoma. On MR imaging, superficial invasion was demonstrated in two patients.

**Pathologic findings**

Surgically resected uterus showed generally soft and friable, broad-based polypoid tumors that filled the endometrial cavity and invaded the myometrium. The cut surface of the tumors was fleshy, variegated, hemorrhagic and necrotic. Microscopically, eight of nine tumors in group 1 and three of four in group 2...

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**Fig. 1.** A 72-year-old woman with history of radiation therapy for stage IIIb cervical carcinoma 17 years ago.

A. Enhanced CT scan reveals distended endometrial cavity with fluid retention. A heterogeneously enhancing solid mass is attached to the right myometrial wall. The myometrium is effaced remarkably.  

B. Axial T1-weighted MR image (500/20) obtained two days after CT scan shows a large endometrial mass of inhomogeneous low signal intensity and fluid of high signal intensity in the uterine cavity. Also noted a tiny hypodense nodule at the Lt anterolateral aspect of uterine cavity.  

C. Gadolinium-enhanced axial T1-weighted image reveals a heterogeneously enhancing solid mass. Note a solitary small nodule attached to contralateral myometrial wall.  

D. Axial T2-weighted image (2000/80) shows an inhomogeneous tumor invading parametrium beyond serosal surface of the myometrium (white arrow), which was confirmed on operation. Another two small nodules arising from the anterior and posterior portion of uterine cavity.
showed endometrial carcinoma intermingled with spindle cells resembling leiomyosarcoma.

In nine patients who had undergone hysterectomy, we were able to analyze the depth of myometrial invasion in resected specimens. MR staging correlated well with pathologic findings in six cases; three in stage I b, two in stage II, and one in stage III, respectively. In three other stage I cases operated on, the depth of myometrial invasion could not be predicted because these patients underwent only CT examination.

In stage I MMMT, cervical stromal tissue showed fibrosis without tumor invasion. In the advanced stage, however, the tumor invaded cervical canal remarkably. There was no correlation between pathologic subtype (heterologous or homologous) and imaging findings.

Discussion

The pathologic diagnosis of MMMT is reserved for only those neoplasms in which there is an admixture of malignant glandular component and malignant stromal element (5, 6). In this study, we have used the term MMMT to mean a carcinoma mixed with either heterologous or homologous sarcoma. As a post-irradiation sequela, heterologous MMMT is known to be more frequent than homologous (1). In our study, all irradiated patients and three of four in the non-irradiated group revealed heterologous types.

Most of these tumors arise spontaneously, but 7-46% of patients received pelvic irradiation for unrelated disease several years before the diagnosis of MMMT (1, 5, 7-13). The latent interval between initial radiation and the diagnosis of MMMT ranges from five to 40 years (median, 16-21). The dosage of radiation ranges from 30 to 50 Gy (6, 12). In our study, the tumor developed 6-17 years (mean, 9.5) after pelvic irradiation of 57-75 Gy in total dosage.

Many authors have suggested an extremely poor prognosis for irradiation-associated MMMT (7, 8), because at initial presentation these tumors are aggressive and show deep myometrial invasion. Our study showed that three of nine patients (33%) in the irradiation-associated group were at stage I, while three of four patients (75%) in the non-irradiated group were at this stage. The reported five-year survival rate is 20-39% (3, 5, 6, 9, 10-12), if the tumor is localized to the uterus, however, this range is 58-75% (3, 5, 6, 11, 13).

As the extent of myometrial invasion is one of the most important prognostic factors (8), it is important to evaluate the extent of the tumor at the time of diagnosis. MR imaging is superior to CT scan in evaluating the depth of myometrial invasion (14, 15). MR images show diffuse low signal intensity with focal hemorrhagic foci on T1-weighted image. On enhanced study the mass shows heterogeneous enhancement. On T2-weighted images, MMMT displays a heterogeneous,

Fig. 2. A 49-year-old woman with history of radiation therapy for cervical carcinoma 7 years ago.

A. Longitudinal sonography of the pelvis shows distended endometrial cavity with an internal inhomogeneous solid mass (calipers). Note small foci of hypoechoic lesions within the solid mass representing necrosis. B: bladder

B. CT scan obtained 4 months later shows rapid growth of a solid mass occupying entire endometrial cavity without surrounding fluid content.

C. Axial T1-weighted image (500/20) shows a heterogeneous endometrial mass of higher signal intensity than that of surrounding myometrium.

D. Axial T2-weighted image (2000/80) shows a mass of high signal intensity with irregular interface between the mass and the junctional zone in left posterolateral aspect representing superficial myometrial invasion. Tumor invasion into the inner half of the myometrium was proved on hysterec-
intermediate or high signal intensity(2, 4). On MR imaging, myometrial invasion can be predicted by the presence of an irregular endometrium-myometrial interface and by the extension of hyperintense tumor into the myometrium(14). In endometrial carcinoma, the accuracy of MR imaging in assessing superficial and deep myometrial invasion was 89% and 54% respectively(15). In our study, six pathologic specimens correlated well with pre-operative MR imaging.

Since the number of MMMT in most series is small, there have been no reports of different imaging findings between these tumors and MMMT not related with irradiation. Shapeero et al. reported seven patients with MMMT and concluded that MR appearances were nonspecific and mimicked endometrial carcinoma; they did not mention a history of previous pelvic irradiation(2). Gross findings of MMMT were reported as a single polypoid mass(70%), multiple polyps(22%), and diffuse plaques(8%) without regard to any history of irradiation(7). In our study, the irradiation-associated group showed a distended endometrial cavity filled with a large amount of fluid, and with a mural polypoid mass(Fig. 1, 2, and 3). Interestingly, in one patient on follow-up study, the amount of fluid decreased as the polypoid mass grew, and eventually the mass occupied the entire endometrial cavity(Fig. 2). In the broad scheme of events, finding a fluid collection in the endometrial cavity associated with a polypoid mass has been well described as one of the imaging findings of endometrial carcinoma(14, 15).

The non-irradiated group in our study, however,

![Fig. 3](image-url) A 54-year-old woman with history of pelvic irradiation for stage II b cervical carcinoma 8 years ago.

A. Axial T1-weighted image (500/20) shows distended endometrial cavity and a solid mass attached to the right myometrial wall. Small high signal intensity medial to main mass represents hemorrhagic foci.

B. Axial T2-weighted image (2000/80) at the same level shows endometrial fluid and ascites posterior to the uterus. An endometrial solid mass deeply invaded the myometrium and extended to the right parametrium, which was pathologically confirmed.

![Fig. 4](image-url) A 21-year-old woman without history of previous pelvic irradiation.

A. Gadolinium-enhanced sagittal T1-weighted image (500/20) reveals no fluid retention in the endometrial cavity. Instead an enhancing mass of intermediate signal intensity occupies the uterine fundus and body.

B. Sagittal T2-weighted image (2000/80) at same level shows an endometrial mass of high signal intensity. Junctional zone is disrupted representing inner myometrial invasion, that was confirmed on following hysterectomy.
showed a solid mass replacing the endometrial cavity without any fluid retention even in the early stage (Fig. 4). These cases cannot be differentiated from endometrial carcinoma or leiomyosarcoma.

The dilated endometrial cavity in patients with irradiation-associated MMMT is attributable to stenosis of the cervical canal resulting from previous pelvic irradiation. As bleeding from a tumor occurs, the cervical stenosis prevents egress of blood from the uterine cavity, and this accounts for the enlarged uterus and cramping pelvic pain (9). This might explain why abdominal distention is much more frequent among patients with irradiation-associated MMMT than the non-irradiated group (5). The latter usually present with vaginal bleeding alone rather than a dilated uterine cavity (5). In our cases, seven of nine irradiated MMMT patients presented with pelvic mass, while all four non-irradiated MMMT presented with vaginal bleeding. Though some of the tumors could be confused with recurrent cervical carcinoma or concomitant endometrial carcinoma, these findings are consistent with the hypothesis that initial findings of distended endometrial cavity with fluid retention and mural mass favor irradiation-associated MMMT, while a massive solid mass replacing the endometrial cavity may denote non-irradiated MMMT. Since the total number of patients in our series is small and does not lend itself to statistical analysis, only a trend suggesting differences between these two groups has emerged; for validation, a large series will be needed.

In conclusion, imaging findings of irradiation-associated MMMT appeared to be different from those of non-irradiated MMMT; where there are initial findings of a distended endometrial cavity filled with fluid and mural mass, one should be alert to the possibility of irradiation-associated MMMT.

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자궁의 혼합 Müller 종양의 CT와 MRI 소견: 방사선치료 후 발생한 MMT와 방사선치료와 관계없이 발생한 MMT와의 감별1

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2 원자력병원 산부인과
3 원자력병원 해부병리과

이미숙·김기환·이태현·진수일·박상윤2·이승숙3

목 적: 골반에 방사선 치료를 받은 적이 있는 환자에서 발생한 MMT의 방사선학적 소견을 분석하고 방사선 치료의 기왕력이 없는 환자에서 발생한 MMT와 비교하여 양자간의 감별점유무에 대해 알아보고자 하였다.

대상 및 방법: 방사선학적으로 MMT로 진단된 환자 중 방사선 치료를 받은 적이 있는 환자 (n=9)를 group 1, 방사선 치료의 기왕력이 없는 환자 (n=4)를 group 2로 나누어, 각각의 CT (n=10)와 MRI (n=8) 소견을 분석하였다. 각 group에서 종양의 크기, 종양의 침윤 범위, 조영 증강의 유무 및 정도, 종양의 내부 구조를 분석하였다.

결 과: 종양의 크기는 group 1 (평균 8.7cm)이 group 2 (평균 5.5cm)보다 큰 경향을 보였다. Group 1 중 8 예에서, 자궁강이 액체로 확장된 소견을 보이고 자궁 세부나 기저부에 고형 종괴의 소견을 보았다. Junctional zone은 소실되고 종괴 내부에 출혈과 괴사로 인한 소견이 보였다. group 2의 모든 예와 group 1 중 1예에서는 고형 종괴가 자궁강을 차지하고 동반된 액체 저류의 소견은 없었다.

결 론: 자궁강이 액체로 확장되고 벽면의 고형종괴 소견은 방사선치료를 받은 적이 있는 환자에서 발생한 MMT에서 주로 관찰되어 방사선 치료의 기왕력이 없는 환자에서 발생한 MMT와 감별에 도움이 되리라 생각한다.
79th Annual Meeting of the American Radium Society (1997/04/30 – 04)

venue: The Plaza New York City, New York, USA.

contact: American Radium Society,
P.O. Box 2348, Merrifield, VA 22116, USA.
(tel: 1-800-3732204; fax: 1-703-6481863)

45th Annual Scientific Meeting of the Radiation Research Society (1997/05/01 – 08)

venue: Providence, RI, USA.

contact: Mark G. Watson, Ex. Secr., Radiation Research Soc.,
2021 Spring Road, Ste. 600, Oak Brook, IL 60521, USA.
(tel: 1-708-5712881; fax: 1-708-5717837)

97th Meeting American Roentgen Ray Society (1997/05/04 – 09)

venue: Hynes Convention Center Boston, MA, USA.

contact: American Roentgen Ray Society,
1891 Preston White Drive, Reston, VA 22091, USA.
(tel: 1-703-6488992; fax: 1-703-2648863)

Annual Brachytherapy Meeting GEC-Estro (1997/05/07)

venue: Stockholm, Sweden.

contact: ESTRO Secretariat, UH Gasthuisberg,
Herestraat 49, B-3000 Leuven, Belgium.
(tel: 32-16-347680; fax: 32-16-347681)

78th Deutscher Roentgenkongress (1997/05/07 – 10)

venue: Wiesbaden, Germany.

contact: Beate v. Waldthausen, Deutsche Roentgenges. e. V.,
Postfach 1336, D-61283 Bad Homburg, Germany.
(tel: 49-6172-488585; fax: 49-6172-488587)

Annual Meeting Society for Pediatric Radiology (1997/05/13 – 18)

venue: St. Louis, MO, USA.

contact: Ms. Jennifer Boylan, Ex. Secr. SPR,
2021 Spring Rod, Ste 600, Oak Brook, IL 60521, USA.
(tel: 1-708-5712197; fax: 1-708-5717837)

The Conference on Thoracic Radiology and Radiology of the Breast (1997/05/14 – 15)

venue: Ivano-Frankivsk, Ukraine.

contact: Dr. V. T. Djomin,
Lomonosova atr. 33/43, Kiev, Ukraine 252022.
(tel: 380-44-2665758; fax: 380-44-2660108)

35th Annual Meeting of the American Society of Neuroradiology (1997/05/16 – 22)

venue: Metro Toronto Conv. Ctr. Toronto, Canada.

contact: Tim Moses or, Lora Tannehill, ASNR,
2210 Midwest Road, Ste 207, Oak Brook, IL 60521, USA.
(tel: 1-708-5740220; fax: 1-708-5740661)

Annual Congress British Institute of Radiology with Med-Ex-Ray Exhibition (1997/05/19 – 21)

venue: Int. Convention Centre Birmingham, United Kingdom.

contact: Miss S. E. Nickson, Bir, 36 Portland Place,
London Win 4AT, United Kingdom.
(tel: 44-171-4367807; fax: 44-171-2553209)

84th Congress & Annual Meeting of the Swiss Society for Medical Radiology (1997/05/22 – 24)

venue: Basel, Switzerland.

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Petersgraben 4, Ch-4031 Basel, Switzerland.
(tel: 41-61-2654385; fax: 41-61-2655351)

34th Annual congress European Society of Pediatric Radiology (1997/05/26 – 30)

venue: Lugano, Switzerland.

contact: Prof. G. Wilms, UZ Gasthuisberg,
Herestraat 49, B -3000 Leuven, Belgium.
(tel: 32-16-343771; fax: 32-16-3437699)

European Course in Neuroradiology – Skull Base (1997/05/31 – 04)

venue: Leuven, Belgium.

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Herestraat 49, B -3000 Leuven, Belgium.
(tel: 32-16-343771; fax: 32-16-3437699)

Sandwichcursus (subject to be defined) (1997/06/03 – 04)

venue: De Jaarbeurs Utrecht, The Netherlands.

contact: Mrs. F. E. Blomendaal, NVvRd,
P.O. Box 8171, 3503 RD Utrecht, The Netherlands.
(tel: 31-30-2474294; fax: 31-30-2474439)

International Congress of Radiation Oncology 1997 (ICRO ‘97) (1997/06/04 – 07)

venue: Beijing, China.

contact: ISRO Office, Mrs. M. Stevens, UH Gasthuisberg,
Radiothe., Herestraat 49, B-3000 Leuven, Belgium.
(tel: 32-16-347685; fax: 32-16-347681)

Sandwichcursus (subject to be defined) (1997/06/05 – 06)

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P.O. Box 8171, 3503 RD Utrecht, The Netherlands.
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5th Annual Congress European Society of Thoracic Imaging (1997/06/06 – 08)

venue: Conrad Hotel Brussels, Belgium.

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Domaine de Sart-Tilman-B35, 4000 Liege 1, Belgium.
(tel: 32-41-667259; fax: 32-41-667224)