

## The size and number is not everything to evaluate the tumor response in gastrointestinal stromal tumors

### Gastrointestinal stromal tümörlerde tümör yanıtı değerlendirilmesinde boyut ve sayı herşey demek değildir

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#### ÖZET

Gastrointestinal stromal tümörler gastrointestinal sistemin en yaygın görülen mezenkimal tümörleridir. Kontrastlı bilgisayarlı tomografi, tedaviye yanıtı değerlendirmede en yaygın kullanılan yöntemdir. Hedefli tedaviler tümör yapısında bazı değişikliklere neden olabilir. Lezyon vaskülaritesinde azalma, kavitasyon ve intratümöral kanama, imatinib tedavisi sonrası hastalarda herhangi bir boyut azalması olmadan bile görülebilen bazı değişikliklerdir. Çelişkili olarak, kistik değişiklik ve intratümöral kanama nedeniyle bazı durumlarda geçici bir boyut artışı görülebilir. Gastrointestinal stromal tümörlerde Choi ve arkadaşları tarafından alternatif tümör yanıt kriterleri geliştirilmiştir. Choi ve arkadaşları Yanıtın değerlendirilmesinde sadece tümör boyutunun değil tümör yoğunluğunun da önemli olduğunu gösterdiler. Bu çalışmada biz gastrointestinal stromal tümör tanısı alan, imatinib ile tedavi edilen 67 yaşında erkek hastayı sunduk. 3 aylık imatinib tedavisinden sonra, yanıt değerlendirilmesinde karaciğer lezyonları progresyon olarak rapor edilmişti.

#### ABSTRACT

Gastrointestinal stromal tumors are the most common mesenchymal tumors of the gastrointestinal tract. Contrast-enhanced computed tomography is the most commonly used for evaluating response to treatment. Targeted therapies may cause some changes in tumor structure. Reduced lesion vascularity, cavitations, and intratumoral hemorrhage are some changes in patients after imatinib therapy, even without any size reduction. Paradoxically, a transient increase in size may be seen in some cases due to cystic change and intratumoral hemorrhage. Alternative tumor response criteria were developed by Choi et al. in gastrointestinal stromal tumor. Choi et al. showed that not only the tumor size but also the tumor density are important in evaluating the response. In this study, we presented a 67-year-old male patient treated with imatinib receiving a gastrointestinal stromal tumor diagnosis. After 3 months of imatinib treatment, liver lesions were reported as progression in response assessment.

Gastrointestinal stromal tumor (GIST) is one of the most common soft tissue sarcoma subtypes; each year ~3,300–6,000 new cases are diagnosed.<sup>1,2</sup> GIST is usually seen in middle age and elderly patients; with ~60% located in the stomach, 30% in the small intestine, and 10% in other regions of the gastrointestinal (GI) tract.<sup>3</sup> Size, mitotic rate, and location of the primary lesion are the most

important prognostic factors.<sup>4</sup> GIST may be increased in size during treatment because of intratumoral hemorrhage or myxoid degeneration. Decreasing in tumor density on computed tomography (CT) is an important early clinical marker of antitumor activity. Once tumors become hypodense (cystic), the size of the lesions may decrease slowly and eventually stabilize.<sup>5,6</sup> Responses can be

observed within 24 hours of starting therapy on PET-CT. <sup>7</sup>

**Table 1:** Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1

Response assessment	RECIST, version 1.1
<b>Target lesions</b>	
<b>CR</b>	Disappearance of all target lesions and reduction in the short axis measurement of all pathologic lymph nodes to $\leq 10$ mm
<b>PR</b>	$\geq 30$ percent decrease in the sum of the longest diameter of the target lesions compared with baseline
<b>PD</b>	$\geq 20$ percent increase of at least 5 mm in the sum of the longest diameters of the target lesions compared with the smallest sum of the longest diameter recorded OR The appearance of new lesions, including those detected by FDG-PET
<b>SD</b>	Neither PR nor PD

CR: complete response; PR: partial response; PD: progressive disease; FDG-PET: fludeoxyglucose-positron emission tomography; SD: stable disease

The 67-year-old male patient was admitted to our hospital to determine the cause of anemia. Heterogeneously enhancing solid mass (11x17 cm) revealed in the pelvic region and multiple metastatic lesions in the liver were determined on abdominal CT (Figure 1,2). The mass was originated from the ileum. GIST was diagnosed as a result of the biopsy of the abdominal mass and liver. Imatinib therapy (400 mg/day) was started. After 3 months of imatinib treatment thoracic and abdominal CT scans were taken. The mass in the pelvic area measured 7x7.5 cm (Figure 3). However, in the liver parenchyma, metastatic lesions were reported as progression by the department of radiology according to RECIST 1.1 criteria (Table 1) (Figure 4). In PET-CT examination there were multiple hypodense lesions in the liver with no FDG uptake (Figure 5). Abdominal CT examination was re-evaluated by Choi criteria (Table 2) (Figure 6,7,8). And then compared tumor density findings was compatible with the partial response. At this

time imatinib therapy (400 mg/day) is still ongoing. There is no disease progression for 10 months. Stable disease is going on.

**Table 2:** Choi criteria.

Response assessment	Choi criteria
<b>CR</b>	Disappearance of all lesions No new lesions
<b>PR</b>	A decrease in size $\geq 10$ or a decrease in tumor attenuation (HU) $\geq 15$ on CT No new lesions No obvious progression of non measurable disease
<b>PD</b>	An increase in tumor size $\geq 10$ and does not meet criteria of PR by tumor attenuation on CT New lesions
<b>SD</b>	Does not meet the above criteria

CR: complete response; PR: partial response; PD: progressive disease; SD: stable disease  
CT: Computed tomography

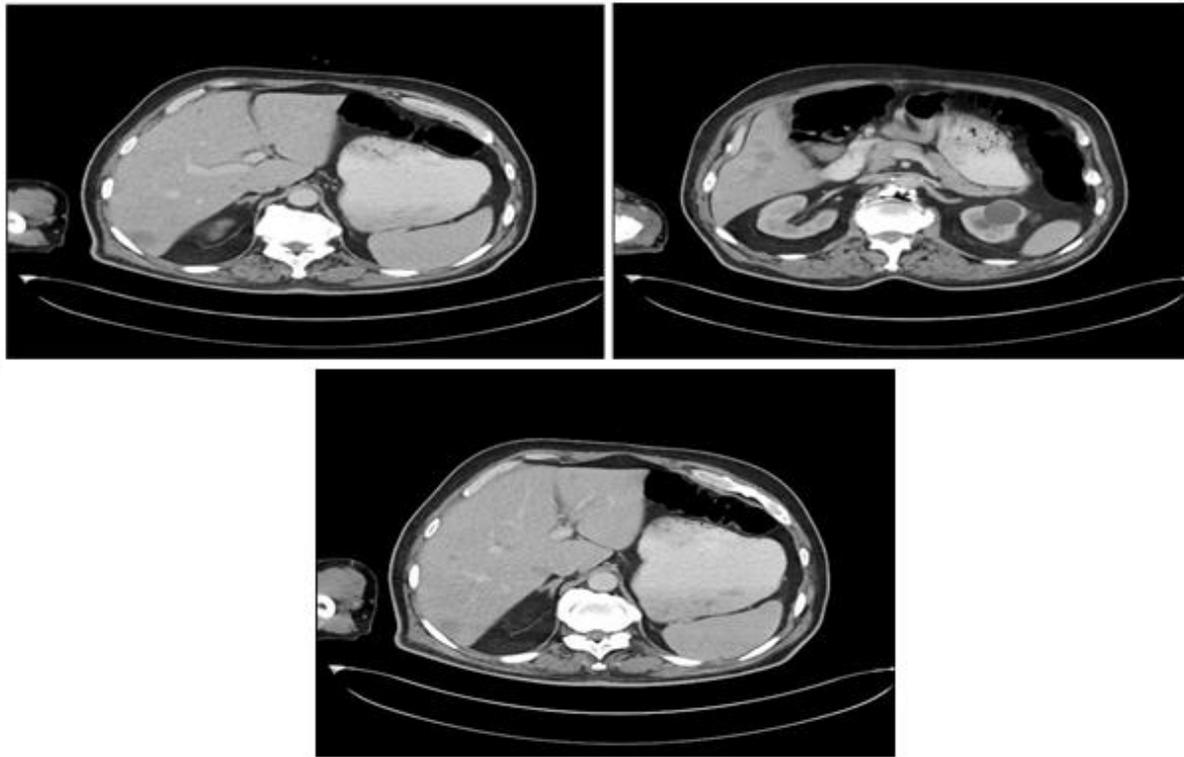
In metastatic GIST; There are differences for evaluating treatment response compared to other solid tumors. For example, late response may occur who have stable disease. A clinical trial performed by Verweij et al. demonstrated that the median time of objective response is four months, a maximal response may be in six months or even longer.<sup>8</sup> In clinical trials performed that PET-CT is able to show an earlier response than CT.<sup>9,10</sup> Treglia et al., demonstrated that PET-CT has a significant value in assessing treatment response in GIST. This modality allows an early evaluation of treatment response and is a strong predictor of clinical outcome.<sup>11</sup> Alternative response assessment criteria (Choi criteria) have been developed in GIST. Investigators at MD Anderson reported that Choi criteria are a better predictor of response to therapy than standard RECIST criteria. Also, they showed that 10 percent decrease in unidimensional tumor size or a 15 percent decrease in tumor density on contrast-enhanced CT scans (Partial response) correlates well with PET scan findings (Table 2).<sup>12,13</sup> Fluid retention is a common side effect of imatinib therapy. Treatment-related fluid retention may be seen as ascites, a pleural effusion, a pericardial effusion, or extensive subcutaneous edema.

New ascites or effusions noted on CT scans can be mistakenly regarded as a new finding of peritoneal disease when the disease is otherwise stable or resolving. This is an important consideration in evaluating the response.<sup>14</sup>

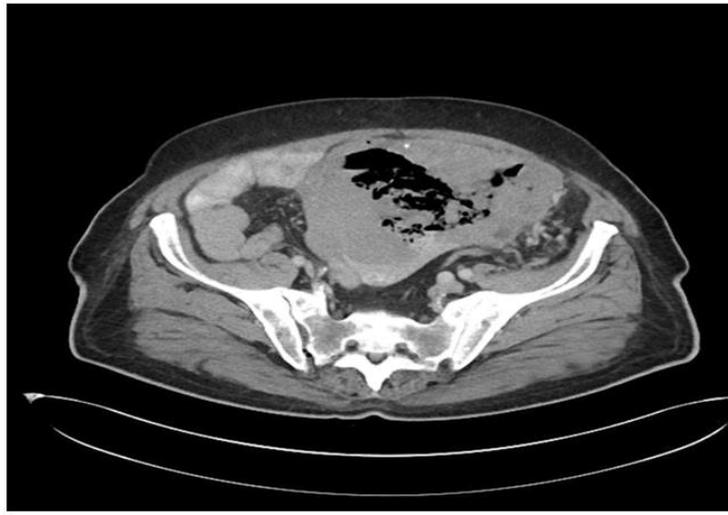
Tumoral lesions may enlarge paradoxically during treatment in GIST. These enlargements can be due to the development of intratumoral hemorrhage or myxoid

degeneration. Enlargement of the tumor does not indicate progression. Also at the beginning uninformed tumoral solid lesions may become cystic and may appear as new lesions in the later months of treatment. In this study, we presented the response evaluation process in our patient with metastatic GIST who received imatinib therapy.

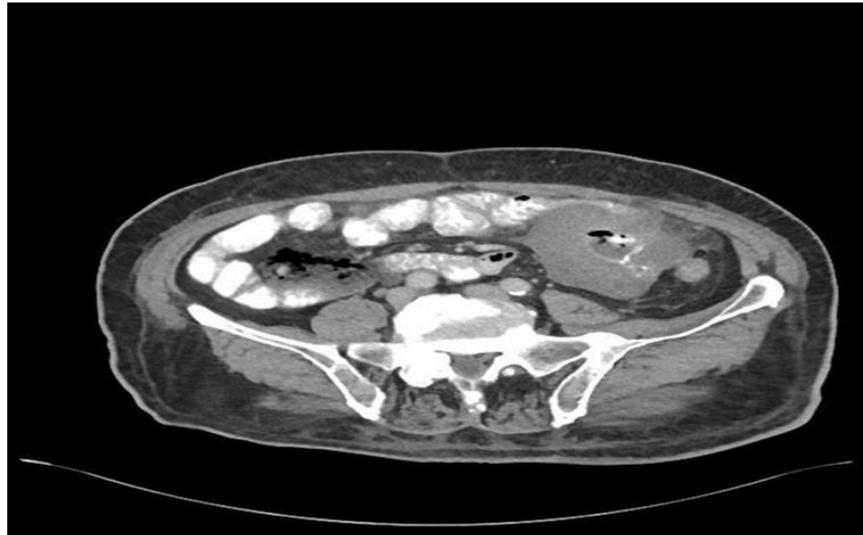
**Conflict of interest:**None



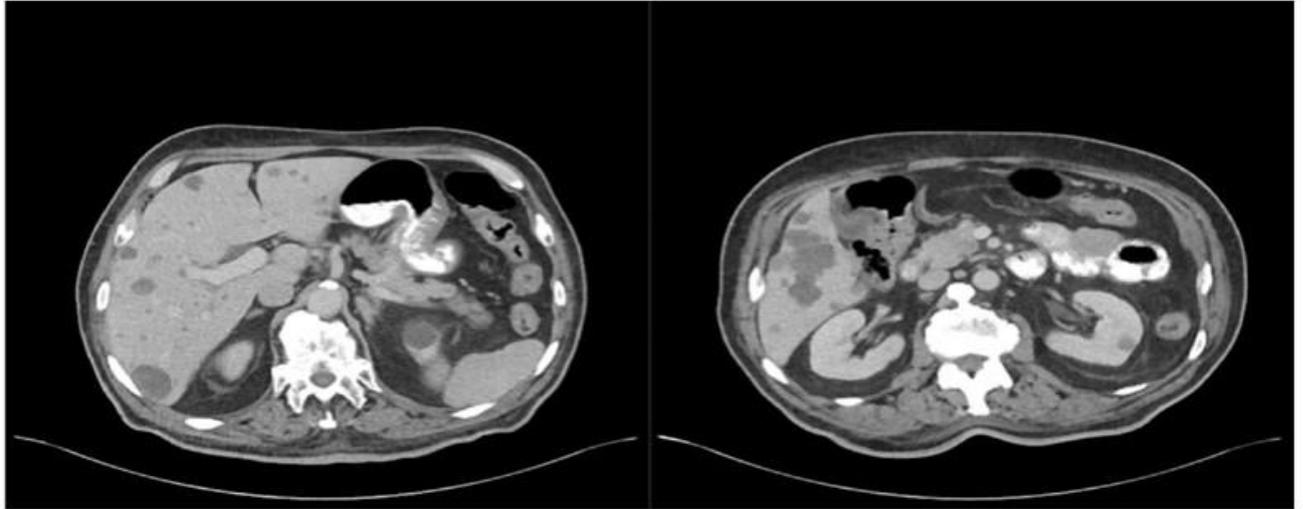
**Figure 1:** Multiple metastatic lesions are seen in left and right lobes of the liver. Before starting treatment of imatinib. A, B: Metastatic lesions in right lobe. C: Metastatic lesions in right and left lobes.



**Figure 2:** Heterogeneous mass (11x17 cm) in the pelvic region of abdomen. The mass was originated from ileum. GIST was diagnosed by biopsy in this primary lesion. (Before starting Imatinib treatment)

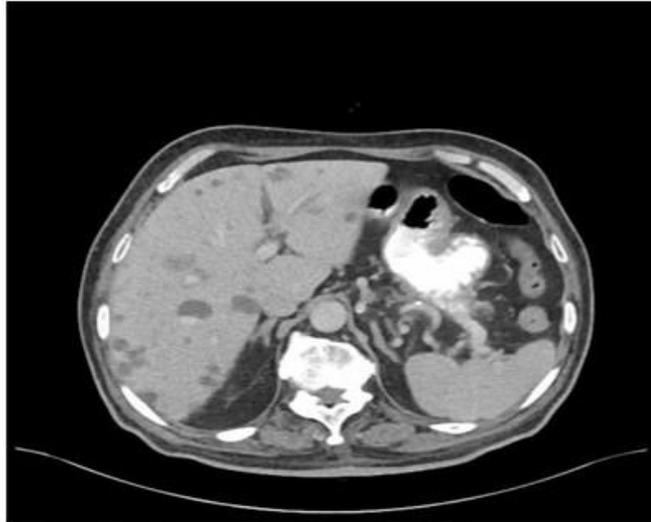


**Figure 3:** The primary, heterogeneous mass dimensions have decreased (7x7.5 cm). Tumor has partial response according to RECIST criteria. (After three month of the imatinib treatment)



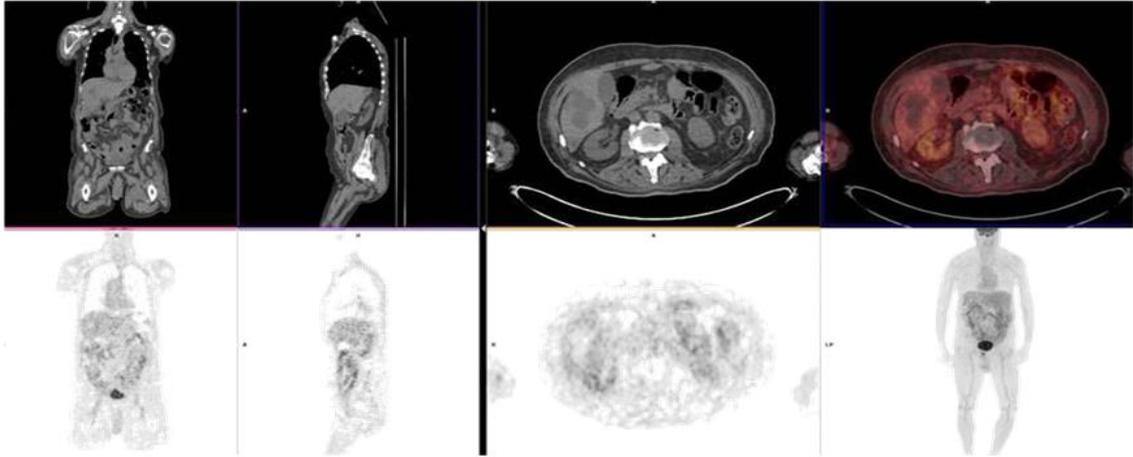
**A** Metastatic lesions in right and left lobe

**B** Metastatic lesions in right lobe



**C:** Metastatic lesions in right and left lobes

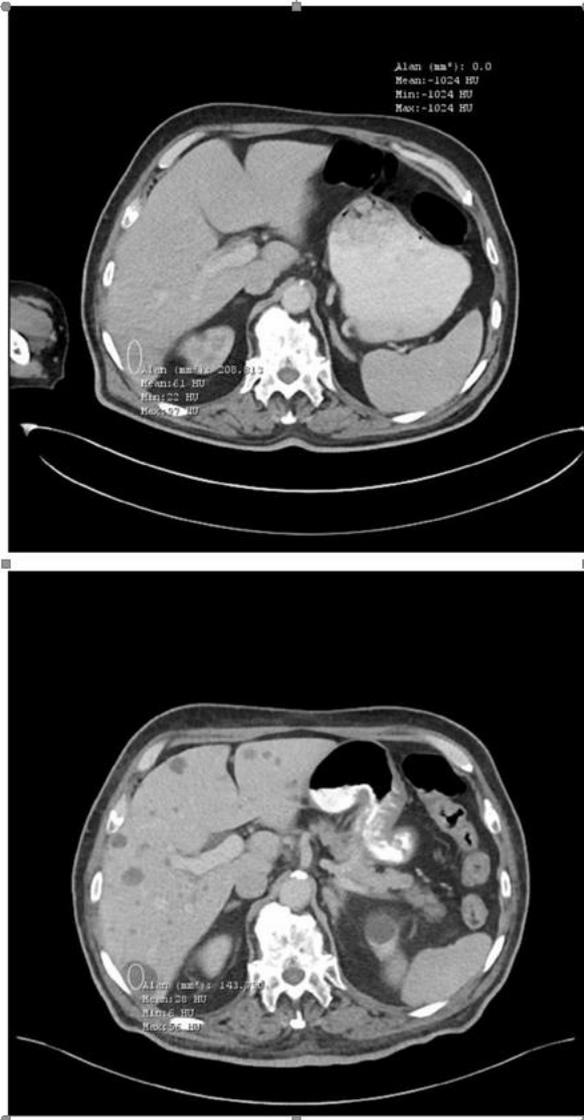
Figure 4: Multipl metastatic lesions are seen in left and right lobes of the liver. Metastatic lesions number and size were increased. It can be interpreted as progression according to RECIST criteria. (After three month of the imatinib treatment.) A,C: Metastatic lesions in right and left lobes. B: Metastatic lesions in right lobe



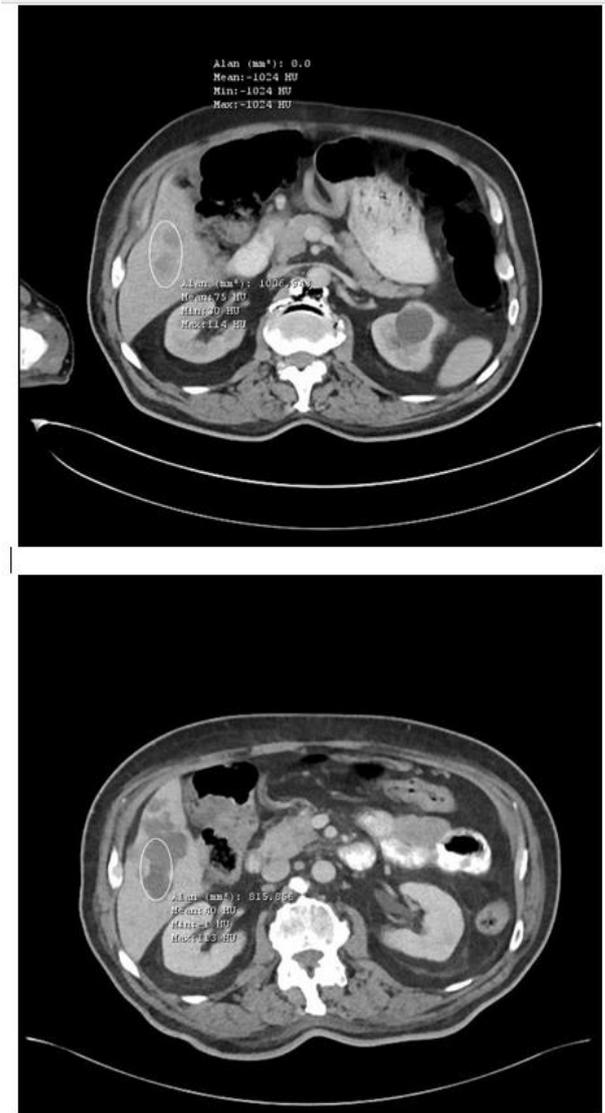
**Figure 5:** FDG uptake is not seen in metastatic lesions. PET CT was performed 3 months after the imatinib therapy



**Figure 6:** Comparison of tumor densities on primary mass before treatment and after 3 months of imatinib treatment. (Before treatment: 57 Hounsfield Units (HU), After 3 months of imatinib treatment: 44 HU) **A:** Tumor density of primary mass before treatment. **B:** Tumor density of primary mass after 3 months of imatinib treatment.



**Figure 7:** Comparison of tumor densities on same metastatic liver lesion before treatment and after 3 months of imatinib treatment. (Before treatment: 61 HU, After 3 months of imatinib treatment: 28 HU)  
A: Tumor density of metastatic liver lesion in right lobe before treatment. B: Tumor density of metastatic liver lesion in right lobe after 3 months of imatinib treatment



**Figure 8 :** Comparison of tumor densities on same metastatic liver lesion before treatment and after 3 months of imatinib treatment. (Before treatment: 75 HU, After 3 months of imatinib treatment: 40 HU)  
A: Tumor density of metastatic liver lesion in right lobe before treatment. B: Tumor density metastatic liver lesion in right lobe after 3 months of imatinib treatment.

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