

Importance of gallium scan restaging for curative treatment of mediastinal lymphomas

In patients with mediastinal lymphoma, gallium-67-citrate single photon emission computed tomography ($^{67}\text{GaSPECT}$) provides unique information on the presence of residual active disease.¹⁻⁵ We provide an updated report on a large cohort of patients whose management following induction therapy was based on routine $^{67}\text{GaSPECT}$ restaging.

Between June 1994 and January 2000, 63 patients with Hodgkin's disease (HD) or aggressive non-Hodgkin's lymphoma (NHL) with initial mediastinal disease were treated at our Institute with induction chemotherapy and radiotherapy. Radiological clinical staging with evaluation of tumor size included computed tomography (CT) and $^{67}\text{GaSPECT}$. CT was monitored at diagnosis, at the end of chemotherapy, and 2 months after radiotherapy; $^{67}\text{GaSPECT}$ was performed at the time of diagnosis and following combination therapy (i.e. 3 months after radiotherapy in order to avoid false negatives).

Thirty-six patients had HD and 27 patients aggressive NHL (27 males, 36 females; median age 35 years, range 19-72 years). All patients were previously untreated. Thirty-six (58%) patients had bulky mediastinal disease. HD patients were treated with ABVD⁶ regimen and patients with aggressive NHL were treated with the MACOP-B⁷ or VNCOP-B⁸ regimen according to their age (< 60 years and \geq 60 years, respectively). One month after the completion of either chemotherapy program, all patients received radiotherapy to the mediastinum.

Complete remission (CR) was defined when a complete regression of all assessable disease had occurred. During the follow-up the $^{67}\text{GaSPECT}$ was performed every six months for the first three years, and every 12 months thereafter. Patients who were $^{67}\text{GaSPECT}^+$ at restaging were therefore considered as having persistence of active disease and underwent further treatment. Irrespective of CT findings, patients who had a $^{67}\text{GaSPECT}$ -restaging received close follow-up without further treatment.

After the combined modality treatment, thirteen out of 63 (21%) patients were $^{67}\text{GaSPECT}^+$ and forty-two (67%) CT⁺. As regards these 42 patients with a positive CT scan, the majority (35/42; 84%) were $^{67}\text{GaSPECT}^-$. Whereas all 35 patients who were $^{67}\text{GaSPECT}^-/\text{CT}^+$ remained in continuous complete remission (CCR), two of the 7 (28%) patients who were $^{67}\text{GaSPECT}^+/\text{CT}^+$ subsequently experienced local relapse (after 11 and 16 months). Despite three cycles of a second-line conventional chemotherapy regimen, they always remained $^{67}\text{GaSPECT}^+$. Among the seven patients who were $^{67}\text{GaSPECT}^+/\text{CT}^+$, four were eligible for autologous bone marrow transplantation: these four patients all subsequently became $^{67}\text{GaSPECT}^-$ after transplantation and are currently in CCR (at 35, 52, 60 and 62 months). The one other patient who was $^{67}\text{GaSPECT}^+/\text{CT}^+$ received no second-line treatment because of advanced age and poor performance status after induction. Nevertheless, he spontaneously became $^{67}\text{GaSPECT}^-$ at 18 months and is currently in CRR after 34 months. The median follow-up for the $^{67}\text{GaSPECT}^+/\text{CT}^+$ and $^{67}\text{GaSPECT}^-/\text{CT}^+$ subsets was 52 and 39 months, respectively. Figure 1 shows the different relapse-free survival (RFS) curves ($p=0.003$).

Among the 21 patients who were CT⁻ after induction, 6 (29%) turned out to be $^{67}\text{GaSPECT}^+$. Of these, only three out of 6 (50%) are currently in CCR, as compared with fourteen of the 15 (93%) in the $^{67}\text{GaSPECT}^-/\text{CT}^-$ subset. In particular, among the three patients aged <60 years who were submitted to ABMT, two subsequently became $^{67}\text{GaSPECT}^-$ and are currently in CCR (at 45 and 72 months); among the three elderly ones who were submitted to conventional second-line chemotherapy, one converted to being $^{67}\text{GaSPECT}^-$ and is currently in CCR (at 58 months). The

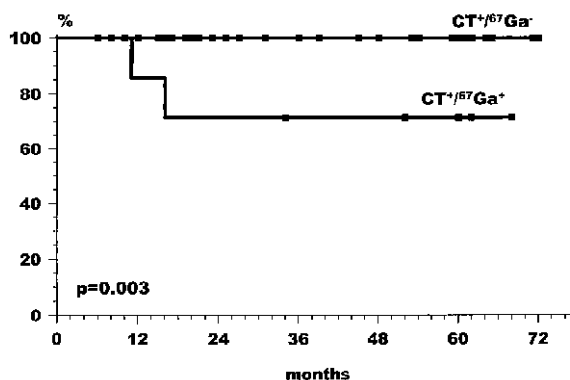


Figure 1. RFS curves comparing $^{67}\text{GaSPECT}^+/\text{CT}^+$ and $^{67}\text{GaSPECT}^-/\text{CT}^+$ subsets.

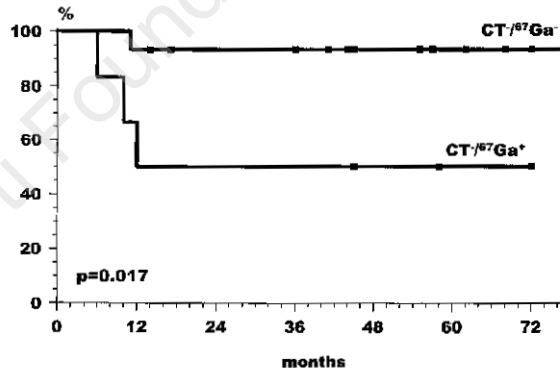


Figure 2. RFS curves comparing $^{67}\text{GaSPECT}^+/\text{CT}^-$ and $^{67}\text{GaSPECT}^-/\text{CT}^-$ subsets.

three patients in the $^{67}\text{GaSPECT}^+/\text{CT}^-$ subset who never became $^{67}\text{GaSPECT}^-$ all experienced local relapse within 12 months in spite of the salvage procedures. On the other hand, one of the 15 patients in the $^{67}\text{GaSPECT}^-/\text{CT}^-$ subset had a mediastinal relapse after 11 months. The median follow-up for the $^{67}\text{GaSPECT}^+/\text{CT}^-$ and $^{67}\text{GaSPECT}^-/\text{CT}^-$ subsets was 45 and 48 months, respectively. Figure 2 shows the different RFS curves ($p=0.017$).

No differences between HD and NHL cases were recorded. The present report provides further indications on the true clinical potential of $^{67}\text{GaSPECT}$ for the management of patients with HD and aggressive NHL with mediastinal disease. As expected, it was possible to stratify patients on the basis of the restaging results provided by $^{67}\text{GaSPECT}$ and CT after induction treatment. $^{67}\text{GaSPECT}$ positivity had a strong impact on RFS, both in the presence and absence of CT positivity.

In conclusion, the present study strongly reinforces the concept that $^{67}\text{GaSPECT}$ must now be considered the restaging method of choice for patients with mediastinal lymphoma.

⁶⁷GaSPECT should thus be routinely used whenever possible for early identification of any residual disease after induction so as to allow timely initiation of the appropriate form of second-line treatment in those patients who really need it.

Pier Luigi Zinzani, Nino Monetti,* Maurizio Zompatori,°
Vittorio Stefani, Stefano Fanti,* Michele Bacarani, Sante Tura
Institute of Hematology and Medical Oncology "Seragnoli"
*Department of Nuclear Medicine, °Radiology Department,
Institute of Radiotherapy "L. Galvani", University of Bologna,
Italy

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Correspondence: Pier Luigi Zinzani, M.D. Istituto di Ematologia e Oncologia Medica "Seragnoli" Policlinico S.Orsola, via Massarenti 9, 40138 Bologna, Italy.
Phone: international +39.031.390413. Fax: international +39.051.6364037. E-mail: plzinzo@med.unibo.it

References

1. Front D, Bar-Shalom R, Mor M, et al. Aggressive non-Hodgkin lymphoma: early prediction of outcome with ⁶⁷Ga scintigraphy. *Radiology* 2000; 214:253-7.
2. Delcambre C, Reman O, Henry-Amar M, et al. Clinical relevance of gallium-67 scintigraphy in lymphoma before and after therapy. *Eur J Nucl Med* 2000; 27:176-84.
3. Gasparini M, Bombardieri E, Castellani M, et al. Gallium-67 scintigraphy evaluation of therapy in non-Hodgkin's lymphoma. *J Nucl Med* 1998; 39:1586-90.
4. Zinzani PL, Zompatori M, Bendandi M, et al. Monitoring bulky mediastinal disease with gallium-67, CT-scan and magnetic resonance imaging in Hodgkin's disease and high-grade non-Hodgkin's lymphoma. *Leuk Lymphoma* 1996; 22:131-5.
5. Zinzani PL, Magagnoli M, Franchi R, et al. Diagnostic role of gallium scanning in the management of lymphoma with mediastinal involvement. *Haematologica* 1999; 84:604-7.
6. Bonadonna G, Zucali R, De Lena M, Valagussa P. Combined chemotherapy (MOPP or ABVD)-radiotherapy approach in advanced Hodgkin's disease. *Cancer Treat Rep* 1977; 61:769-77.
7. Klimo P, Connors JM. MACOP-B chemotherapy for the treatment of diffuse large-cell lymphoma. *Ann Intern Med* 1985; 102:596-602.
8. Zinzani PL, Storti S, Zaccaria A, et al. Elderly aggressive-histology non-Hodgkin's lymphoma: first-line VNCOP-B regimen experience on 350 patients. *Blood* 1999; 94:33-8.