

**THE AUTHORS REPLY:** All patients enrolled in our study were eligible for surgical prostatectomy — that is, they did not have clinical or CT evidence of nodal metastases. In 5 of the 80 patients (6 percent of the study group), lymphotropic nanoparticle-enhanced MRI suggested the presence of solitary metastases in selected nonenlarged lymph nodes (mean nodal diameter, 7.8 mm). These specific lymph nodes were then sampled by CT-guided biopsy, revealing metastases in all five patients. Because of the positive pathological findings, these patients did not undergo additional surgery. These results indicate that patients with solitary lymph-node metastases may be spared surgical exploration.

The goal of our study was not to determine the correct extent of surgical lymph-node dissection, but rather to determine the accuracy of lymphotropic nanoparticle-enhanced MRI in the staging of prostate cancer. We agree with the assessment by Dr. Yaes that more extensive dissection will yield more lymph nodes and will therefore reveal additional metastases (surgery has a higher sensitivity).<sup>1</sup> Because more extensive dissection is also associated with higher morbidity,<sup>2</sup> there is some debate over the appropriate extent of dissection of pelvic lymph nodes.<sup>2</sup> Furthermore, half of patients with newly diagnosed prostate cancer consider nonsurgical approaches to treatment (i.e., radiation therapy, observation, or cryotherapy), and they are deprived of an accurate evaluation of their lymph-node status.

Our study shows that the criteria used in traditional image analysis (size, shape, and clustering) have low accuracy,<sup>3</sup> and that nanoparticle-enhanced MRI has exquisitely high sensitivity. Because of the

high negative predictive value of the technique we described (100 percent) in a patient-by-patient analysis and 97.8 percent in a node-by-node analysis, one can argue that in patients with negative MRI studies, no dissection should be performed at all.<sup>4</sup> In patients with positive MRI findings in small nodes (or nodes in the internal iliac region), either a more extensive dissection or a CT-guided biopsy may be performed. Because most modern MRI systems allow extended pelvic coverage at high spatial resolution, an MRI staging procedure also surveys lymph nodes far beyond the fields of extended surgical resection; this may be of additional benefit to patients and may improve their chance for a cure.

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## Chemotherapy for Hodgkin's Disease

**TO THE EDITOR:** In the study by Diehl et al. (June 12 issue),<sup>1</sup> the median duration of chemotherapy from the first to the last day of drug administration in the group assigned to cyclophosphamide, vincristine, procarbazine, and prednisone alternating with doxorubicin, bleomycin, vinblastine, and dacarbazine (COPP-ABVD) was 46.3 weeks, as compared with 24.4 in the group assigned to bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, and prednisone (BEACOPP) and 24.7 in the increased-dose BEACOPP group. Since the duration of treatment in the COPP-ABVD group was twice that in the BEACOPP group, all that one can conclude from the study is that the more frequent

administration of chemotherapeutic agents resulted in an advantage in terms of freedom from treatment failure, rather than that the doses or the agents in BEACOPP are superior to those in COPP-ABVD. It could well be that the results of COPP-ABVD given at 24-day intervals or at the planned 30-day intervals would be equivalent to those achieved with increased-dose BEACOPP. This question warrants investigation, particularly in view of the 2.5 percent incidence of secondary leukemia in the increased-dose BEACOPP group.

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1. Diehl V, Franklin J, Pfreundschuh M, et al. Standard and increase-dose BEACOPP chemotherapy compared with COPP-ABVD for advanced Hodgkin's disease. *N Engl J Med* 2003;348:2386-95.

**THE AUTHORS REPLY:** First, we made an error in the median duration of COPP-ABVD chemotherapy that is quoted by Dr. Ekert; it should have been 33.4 weeks instead of 46.3 weeks, as printed in our article. Nevertheless, the duration of the COPP-ABVD therapy was still 36 percent greater than that of the BEACOPP therapies (24.4 and 24.7 weeks in the BEACOPP and increased-dose BEACOPP groups, respectively).

Dr. Ekert correctly remarks that the accelerated administration of drugs may have contributed to the increased efficacy of BEACOPP as compared with COPP-ABVD. But the substitution of drugs (etoposide instead of vinblastine and dacarbazine) or

synergetic effects between drugs may also have contributed to the difference in efficacy between COPP-ABVD and standard BEACOPP therapy. The relative importance of these factors is not clarified by our results. The further improvement in results from standard to increased-dose BEACOPP therapy can only be due to the escalation of the doses, since other factors were the same in these two treatment groups. Thus, it is clear (from the data in Table 4 of our article) that most of the improvement in terms of freedom from treatment failure with increased-dose BEACOPP therapy as compared with COPP-ABVD therapy is attributable to the doses used.

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## Radiotherapy for Advanced Hodgkin's Disease

**TO THE EDITOR:** We disagree with Aleman et al. (June 12 issue)<sup>1</sup> that involved-field radiotherapy does not improve the outcome after a complete response to chemotherapy in patients with advanced Hodgkin's lymphoma. The authors used two additional cycles of mechlorethamine, vincristine, procarbazine, prednisone, doxorubicin, bleomycin, and vinblastine (MOPP-ABV) as consolidation chemotherapy after a complete response had been achieved. Not surprisingly, involved-field radiotherapy failed to improve the outcome. Had they performed randomization immediately after the achievement of a complete response, the benefit of radiation might have been evident.

The Children's Cancer Group (CCG) trial,<sup>2</sup> in which 501 patients with a complete response were randomly assigned to involved-field radiotherapy or to observation, was closed early because there were significantly more relapses in the group assigned to chemotherapy alone (three-year event-free survival of 93 percent, vs. 85 percent with involved-field radiotherapy;  $P=0.002$ , according to an "as-treated" analysis). Our own randomized trial (unpublished data) comparing consolidation radiotherapy with observation in 179 patients in whom a complete response was achieved with six cycles of doxorubicin, bleomycin, vinblastine, and dacarbazine (ABVD) shows an improvement in the rates of event-free survival and overall survival at eight years in the radiotherapy group.

In major studies such as those conducted at Stanford University and the National Cancer Institute in Milan, Italy, radiotherapy has been part of the standard protocol treatment for advanced Hodgkin's disease. To quote Prosnitz, "Consolidation radiation for advanced Hodgkin's lymphoma is thus still alive."<sup>3</sup>

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**THE AUTHORS REPLY:** We agree with Dr. Gupta and colleagues that consolidation radiation is not dead; however, the challenge is to select the patients who require radiotherapy. The European Organization for Research and Treatment of Cancer Lymphoma (EORTC) trial was designed to evaluate radiotherapy in patients with advanced Hodgkin's lymphoma