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Introduction to the Fifth Conference on Radioimmunodetection and Radioimmunotherapy of Cancer[1]

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The use of radioactive antibodies in cancer imaging (or RAID)[3] and in therapy (or RAIT) has been advancing for many years (1–8), particularly because the advent of hybridomas for monoclonal antibody production (9) has facilitated the development of a large number of diverse anticancer antibodies. The ability to target and image tumors by RAID depends on a positive ratio between tumor cpm and cpm in adjacent normal tissues or in circulating blood, which can in turn be distinguished by nuclear γ cameras. This has been accomplished, leading to an abundance of radiolabeled antibodies of different species, specificities, and forms, and with diverse labels. A first generation commercial imaging product involved an intact, pancarcinoma antibody (B72.3) labeled with ^{111}In (10). This required imaging after several days and resulted in poor discrimination of tumors in the liver because of the accretion of the radionuclide by normal liver (10). Subsequent developments involved the use of ^{99m}Tc as the isotope of choice and smaller targeting molecules, including monovalent fragments, subfragments (such as single-chain antigen-binding Fvs), and even receptor-binding peptides, such as somatostatin peptides. The smaller molecules not only offer the opportunity of earlier and more rapid tumor targeting and imaging but also a reduced immunogenicity in patients. This conference, and the past four since 1979 (11–14), have recorded these developments and the intriguing opportunities for a more functional diagnosis of malignant lesions, whereby a single study can reveal various sites of spread, including soft-tissue visceral organs, bone, and even bone marrow. Often, a multitude of radiological modalities, based on anatomical and not biological features, are required for similar staging and disclosure of viable tumor. How small can we make such targeting molecules, and how fast and how small can we image tumors in a practical setting? And how can we use this new modality in combination with the traditional anatomical imaging methods, or perhaps with other functional tests, such as positron-emission tomography? Unfortunately, the current political debate involving managed care and cost containment appears to be stifling the development of these technologies, particularly at a commercial level, even before such questions can be studied. Yet, the answers are needed in order to justify the further pursuit of these diagnostic approaches.

Perhaps the most obvious effect of the development and study of RAID is RAIT, which involves both the selective targeting of cancer and the concomitant delivery of cytotoxic radiation. RAIT has experienced three basic problems: inadequate antibody accretion resulting in low radiation doses to tumor; dose-limiting myelotoxicity; and murine antibody immunogenicity (2, 8, 15). The first problem has been the most challenging because myelotoxicity can be mitigated or controlled by autologous bone marrow or stem cell grafting, and/or the use of hematopoietic cytokines, whereas the evocation of antimurine antibodies can be reduced or prevented by replacing rodent antibodies with humanized forms or totally human immunoglobulins. Increasing antibody accretion and targeting higher doses of the therapeutic radionuclide are being pursued by enhancing the expression of the target antigen or by various pretargeting procedures. Finally, different radionuclides, linkers, and antibody forms are being developed as improvements for RAIT, whereas a better selection of tumor types and stages, as well as therapy schedules and antibody dose, also appear to influence the prospects for this new therapeutic modality. Many of these issues are addressed in the articles presented at this conference, and as such represent the current status of this subject from a truly multidisciplinary perspective. This is witnessed best in the RAIT of lymphomas, where a multidisciplinary approach has resulted in impressive and sustained responses in chemotherapy-refractive cases by various protocols and antibodies. This encourages our diligence and optimism to apply similar principles to treat the more ominous solid tumors. At the very least, RAIT may prove of value in combination with other therapeutic modalities, but proving this will require complex and extensive clinical trials.

The papers presented herein are based on the oral or poster presentations of the conference, and were completed thereafter as original articles or overviews in accordance with the style of the journal. The manuscripts were critically reviewed by the program committee, the members of which are shown in Fig. 1, and to whom I am indebted, not only for contributing to the development of the program, but very much for their painstaking editorial efforts.

Fig. 1. Conference's Program Committee. Standing, left to right: Steven M. Larson, Barry W. Wessels, Claude F. Meares, Donald J. Hnatowich, Donald J. Buchsbaum; seated, left to right: Gerald L. DeNardo, Susan J. Knox, Jeffrey Schlom, David M. Goldenberg, Ralph A. Reisfeld, and Margaret A. Tempero.

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[3] The abbreviations used are: RAID, radioimmunodetection; RAIT, radioimmunotherapy.

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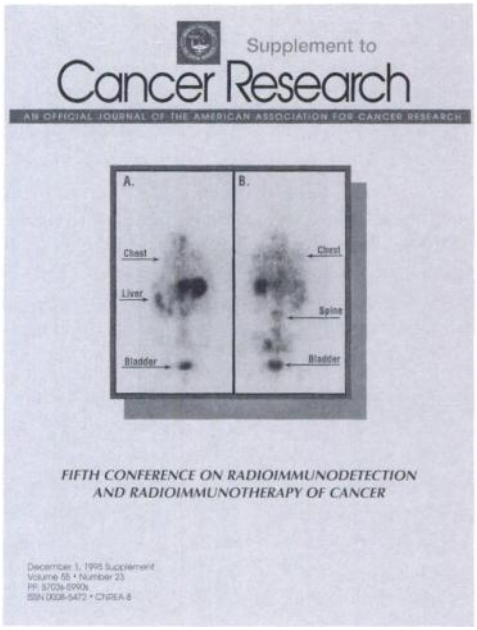
COVER LEGEND



Shown are anterior (*A*) and posterior (*B*) whole-body scans from Figure 3 of the article by Juweid *et al.*, "Targeting and initial radioimmunotherapy of medullary thyroid carcinoma with ^{131}I-labeled monoclonal antibodies to carcinoembryonic antigen," found in this Supplement (pp. 5946s–5951s). Both diffuse and focal sites of medullary thyroid cancer were localized by a radiolabeled antibody to carcinoembryonic antigen, depicting the extent of disease in this patient by means of a single imaging study.

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