The ''Third-Best'' Strategy for Treating Head and Neck Cancer

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There are three basic strategies in the war against head and neck squamous cell cancer. Prevention is the first (so stop drinking excessively and smoking at all if you engage in these self-destructive behaviors). Killing the cancer completely the first time it is treated is the second. The third "best" strategy, salvage of initial treatment failures, is a weak fallback position that easily could be characterized as the worst. Nevertheless, in an attempt to preserve function and cosmesis, patients with head and neck cancers sometimes accept treatment plans that have an incremental chance of local failure and diminished chance of survival to avoid what might be viewed as catastrophic and potentially unacceptable consequences of radical treatment for cure. This trade-off is supported by the concept that a treatment failure can be salvaged with curative intent at a cost of still acceptable cosmetic and functional losses. All physicians who treat head and neck cancer realize salvage comes at a considerable cost in terms of increased morbidity and markedly diminished chances of disease-free survival at most primary sites.

The larynx is an interesting exception to the dim prospects of successful salvage therapy. A primary site recurrence there, discovered while the tumor is confined to the larynx, is quite likely to be cured by salvage laryngectomy. The laryngeal recurrence is still in a "box" that can be removed with an oncologically sound surgical procedure that is relatively easy to perform. Surgical salvage elsewhere is less certain and in some cases (eg, nasopharyngeal carcinoma) essentially impossible because of difficulties in clearance of tumor margins. When tumor recurs, it will be admixed with scar in otherwise deformed tissues and may be biologically more aggressive and apt to spread along nerves and vessels. Failure at the primary site then must be discovered early, before its margins become untreatably diffused into surrounding tissues, if there is to be a reasonable hope for successful salvage.

Since the early 1990s, radionuclide studies have had a recognized potential in the detection of recurrent cancer. In this issue of the *AJNR*, Mukherji et al (page 1215) confirm the value of another tool in the fight to improve salvage of recurrent head and neck cancer. Their study clearly supports the work of others suggesting that thallium-201 single-photon emission CT (SPECT) imaging is useful for identifying multiple head and neck lesion sites and seems to be a reasonable alternative to the less available positron-based imaging agents. This is an important contribution, for even with coincidence techniques and hardware improvements in SPECT imaging of positron emitters, studies such as ^{18}F-flurodeoxyglucose-SPECT are more difficult to perform logistically and are more expensive than those techniques using thallium-201. This tool can and should be used selectively, as the article suggests.

Typically Mukherji et al report greater accuracy of radionuclide techniques for confirmation of recurrence as compared to CT. Much of this is owing to the lack of a post-therapy CT baseline and "conservative" CT interpretation. These points are illustrated in Figure 2 (page 1218) in which a normal asymmetry in the palatine tonsil is read as positive on the CT study. A lack of change from baseline or acceptance of this common normal variation would have improved the accuracy of CT in the study. Nevertheless, their experience and criteria likely match or exceed that generally available, so that their report is accurate within the bounds of their experimental design and the general practice of oncologic imaging in head and neck cancer patients.

Another problem with the detection of recurrent head and neck squamous cell cancer is highlighted in the article. The investigators chose to study only those patients with clinical symptoms of recurrence. Limiting an investigation to this population often means that the patient is less likely to receive salvage therapy than those whose recurrence is detected before becoming symptomatic. Pain, a common symptom of recurrence, may be caused by ulceration. Pain also can arise from disease invasion into nerves, deep musculature, and bone. In other words, symptoms often manifest late. Ulceration or growth of a mass at the primary site is often the tip of an untreatable iceberg. The authors correctly underscore that their article does not address surveillance as an attempt to detect asymptomatic recurrence. These are the people we are far more likely to identify for salvage therapy successfully.

Now that we understand the tools available for detecting asymptomatic recurrence to include CT, MR imaging, and at least two radionuclide techniques, we must begin to apply these as part of our "third-best strategy" in the war against head and neck cancer. Patients at moderate or high risk for recurrence can be identified based on pretreatment imaging and clinical criteria. These patients should have baseline post-treatment studies about 3 months after completion of therapy. The choice of study at this time is not clear, but it seems that either CT or radionuclide studies should suffice. There is no reliable reported experience with MR imaging to date regarding this issue, but it should work as well. It is very likely that a CT baseline study, showing normal post-treatment changes, will correlate with a 90% to 95% chance of local control. A second follow-up study 6 months after com-

pletion of initial therapy, showing stable post-treatment changes or no significant focal accumulation of tracer on CT, will raise the likelihood of local control to nearly 100%. The corollary of this suggested scenario is that progressive imaging changes or focal tracer accumulation will indicate recurrence in about 75% or more of the cases in which those findings occur. With such high positive and negative predictive values, biopsy, with its attendant risks, should be performed only when confronted with a very high likelihood of recurrent tumor. This group will have been triaged on the basis of a pretreatment risk profile and objective post-treatment surveillance studies.

This is not a plea for imaging all patients treated for head and neck cancer. Such a suggestion would be economically irresponsible. It is a plea for the logical and judicious application of powerful imaging tools to help improve the salvage rate and reduce the morbidity of treatment for recurrent head and neck squamous cell cancer. This will become more important as targeted nonsurgical salvage therapies become more widely available in the near future.

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MR Perfusion Imaging

During the last 10 years, a variety of MR techniques have been developed that can provide images of cerebral perfusion (1). These approaches include those that require the injection of paramagnetic contrast agents (bolus-tracking approaches) as well as those that magnetically tag water in arterial blood as it moves into the brain. The effects of ''tagged'' arterial water on brain MR images can be used to calculate quantitative CBF images that can be expressed in classical physiologic units (ie, cc/l00 g/min). The major drawback to these tagging techniques is that, with the current technology, they are rather insensitive and require relatively long imaging times (≈10 minutes). Given this restriction, it is unlikely that MR arterial spin-tagging approaches will be applied to the clinical evaluation of acute stroke in the near future. Nevertheless, they could play an important role in the clinical evaluation of cerebrovascular diseases that provide a longer diagnostic ''window,'' especially for those that require absolute quantitation.

Following the quantitative CBF response to cerebrovascular challenges is one scenario in which MR spin-tagging flow approaches could be very useful. Samuels et al (2) employed the MR spin-tagging response to acetazolamide challenge to study middle cerebral artery stenosis, and used the results to characterize specific patterns of impaired perfusion. In this issue of the *AJNR*, Kastrup et al (page 1233) suggest the use of MR arterial spin-tagging approaches with another variant of the cerebrovascular challenge—breath-holding. Kastrup and colleagues demonstrate that breath-holding can provide reproducible changes in CBF in control subjects that can be followed accurately, both regionally and globally, using MR spin-tagging techniques. The advantage of the breath-hold approach is that it obviates the need for acetazolamide injection or CO_2 inhalation; the disadvantage is that it cannot be used for patients with impaired respiratory function. Both Samuels et al and Kastrup et al underscore the importance of obtaining ancillary data (eg, T_1 relaxation time images) to enable MR spin-tagging data to be interpreted in terms of absolute CBF values. This ability to quantify CBF absolutely is potentially of great clinical importance.

Functional MR (fMR) imaging approaches using blood oxygen level dependent (BOLD) effects also have been used to follow the response to cerebrovascular challenges. BOLD approaches are more sensitive than MR spin-tagging approaches. Kastrup et al emphasize, however, that BOLD results are harder to interpret because fMR imaging responds to changes in various physiologic parameters (eg, CBF, cerebral blood volume, and cerebral oxygen consumption), wheras MR spin-tagging responds primarily to changes in CBF. Nevertheless, MR arterial spin-tagging approaches also present problems in quantitation of CBF. For example, calculated CBF values will be artifactually low when arterial transit times are abnormally long, which might occur in compromised brain regions that have extensive collateral circulation. This issue could be examined using MR bolus-tracking approaches (1), which can give information on arterial transit times in compromised brain areas. Further validation of the quantitative ability of the arterial spin-tagging technique is needed before the results can be applied to individual patients.

The results of Kastrup et al and Samuels et al demonstrate the usefulness of MR arterial spin-tagging approaches for studies of cerebrovascular reserve. These approaches have a number of advantages over other techniques (eg, PET, SPECT, CT, etc); they are noninvasive, easily repeatable, and have relatively good spatial resolution. In the near future, a number of technical advances, such as phased-array head coils and higher magnetic field strengths, undoubtedly will increase the sensitivity of MR arterial spin-tagging approaches, and could make them viable for routine clinical studies of cerebrovascular disease.

An interesting sideline to these studies of physiologic perturbations of CBF is the subtlety and