head and neck coil has considerable appeal, and such "combo coils" will soon be widely used. At the very least, the current "conventional" cervical-cranial MRA techniques can be supplemented with the technique described by LeClerc et al for evaluation of the aortic arch and proximal cervical vasculature. Second, with further technical development, it is likely that coverage can be extended to allow visualization of the ostia and the carotid siphons in one acquisition. Newer contrast agents that do not exit the intravascular space will optimize the ability to do repeated MR sequences after only a single injection, thus providing the "payoff" of very rapid coronal slab sequences obtained sequentially, while maintaining significantly high intravascular signal to limit flow-related artifacts. Thus, LeClerc et al take another step up the stairway, the top of which is the complete replacement of conventional angiography with MRA for evaluation of cerebrovascular disease.

MICHAEL BRANT-ZAWADZKI, MD
Hoag Memorial Hospital Presbyterian
Newport Beach, California

Detection of Perineural Spread: Fat Is a Friend

One could easily argue that the search for perineural tumor spread is the most important task of the radiologist examining a patient with head and neck carcinoma.

Certainly the description of a primary tumor site is important. The relationship of tumor to bone has definite implications in surgical and radiation treatment planning. Many imaging findings alter the surgical plan, but adjustments, though important, tend to be relatively minor. Nodal metastases are a definite determinant of prognosis, but the changes in therapy effected by imaging definition of nodal metastasis are relatively few. The discovery of a tumor that follows a nerve to or through the skull base, however, has an immediate and profound effect on the perception of a patient's disease. The chance for surgical cure plummets, long-term prognosis is significantly changed, and alternative therapies are considered. Detection of perineural spread is crucial. The findings can be very subtle, and the radiologist must seek out any help available.

In any discussion of perineural spread, terminology is important. *Perineural tumor spread* must be distinguished from the designation *perineural tumor* that can be found in the histopathologic report of a primary lesion. The report of perineural tumor in a pathologic report indicates the relationship of tumor to a nerve. This designation may have an effect on prognosis, but does not necessarily imply that the tumor has left the primary area. In perineural tumor spread, the tumor actually appears to use the nerve as a conduit, selectively following the nerve away from the primary site. The tumor moves through the skull base along the same path as the affected nerve. This route allows apparent distant tumor spread because tissues in between remain relatively undistorted.

Ginsberg and DeMonte in this issue of the *American Journal of Neuroradiology* (page 1417) give an excellent demonstration of one of the most important of these perineural pathways: the second division of the trigeminal nerve from palate to pterygopalatine fossa through foramen rotundum to Meckel's cave. Their superb images show the key findings of perineural tumor spread. There is enlargement of the affected foramen, enhancement of the nerve, mass effect in the Meckel's cave region, and obliteration of the fat in the pterygopalatine fossa. I would like to emphasize the importance of this last finding: obliteration of normal fat just external to the neural foramen.

Each of the major head and neck neural pathways transit some amount of fat immediately external to the skull base. The first division of the trigeminal (ophthalmic) neural pathway, which potentially carries tumor from the lacrimal gland, passes through the fat of the superior orbital fissure. The second division trigeminal (maxillary), with connections to the face, palate, and maxillary sinus, must traverse the fat-filled pterygopalatine fossa just external to the foramen rotundum. The third division (mandibular) can carry tumor from connections of the submandibular gland, parotid gland, or potentially, the oral cavity through the foramen ovale. Immediately below the foramen ovale, a fat pad sits just medial to the lateral pterygoid muscle. Tumor following the path of this nerve must traverse this fat before entering the skull base. The facial nerve passes though the fat of the stylomastoid foramen before penetrating the temporal bone. The hypoglossal and glossopharyngeal nerves pass through a small amount of fat as they follow the carotid and jugular just below the skull base.

Tumor has an appearance very different from fat on both CT and on T1-weighted MR images. In our experience this fat is, therefore, very sensitive to tumor spread. An enlarging nerve obliterates that fat so tumor can be detected. Conversely, demonstration of an intact fat pad is a reassuring finding, indicating strongly that the tumor has not passed the fat pad. Thus, the radiologist should be aware not only of the important neural pathways and the foramen that each traverses but also of the fat pad or fossa sitting immediately external to the particular foramen. Obliteration of this fat is often the first, and perhaps the easiest, finding for the radiologist to appreciate.

Which fat planes or pads are most crucial? This certainly depends on the site of the primary tumor in question. Although many tumors such as lymphoma,

melanoma, and squamous cell carcinoma spread along nerves, in our experience and in the current study, adenoid cystic carcinoma is the most common traveler along the perineural pathway. These tumors arise in salivary glands both major and minor as well as in the lacrimal glands. Neural connections from these areas are of obvious importance. The foramen ovale and the stylomastoid foramen are the key transit points from the parotid. The highest concentration of minor salivary glands in the body is in the posterior roof of the mouth, and adenoid cystic carcinoma frequently originates in this location. The pterygopalatine fossa becomes an extremely important landmark as shown in the current article.

The anatomy of the head and neck is indeed complex. Following neural pathways through the region can be an arduous task. Demonstration of an enlarged foramen, an enhancing nerve, or an enlarged cavernous sinus is indeed ominous. The fat planes adjacent to the skull base are equally important and deserve the same understanding and scrutiny. Indeed, when searching for perineural tumor spread, as in many situations in head and neck imaging, fat is truly a friend.

HUGH D. CURTIN, M.D.
Massachusetts Eye and Ear Infirmary, Boston, MA

No Drug Is Benign

Despite the excellent safety record of gadolinium-based compounds for enhanced MR imaging, the potential neurotoxic effects of these drugs are not completely understood. Normally, the blood-brain barrier protects cerebral tissue from foreign chemicals and the overaccumulation of native ones. A variety of pathogenic processes are known to heighten the permeability of the blood-brain barrier, however, allowing a significant increase in the local concentration of a given pharmacologic compound. Creating reproducible and consistent models for the study of the compromised blood-brain barrier remains challenging. Obviously, histologic analysis of cerebral tissue after administration of contrast medium must be performed in an experimental animal rather than a human subject. Examination of animal tissue with an intact blood-brain barrier does not provide insight into gadolinium-induced toxicity, and the results of induced blood-brain barrier compromise are often inconsistent and nonquantitative.

Ray et al in this issue of the *American Journal of Neuroradiology* (page 1455) describe the use of the intraventricular injection model as a reproducible and consistent way of studying the effects of the local accumulation of a compound that may diffuse into the cerebral parenchyma after injection. This type of testing has always been performed for drugs, such as myelographic compounds, intended for intrathecal and intraventricular space injection. While the gadolinium-based agents were initially developed for intravenous injection, other methods of administration are well known. Ray et al do not cite the results of any tests initiated by pharmaceutical developers that examined the effects of gadolinium-based compounds after intrathecal or intraventricular injection in the experimental animal. These tests may have been carried out previously; the manufacturer of the contrast material administered in the present study was interested enough in this line of investigation to fund the project.

The results obtained by Ray et al. indicate that, although the effects of gadopentetate dimeglumine and gadodiamide are similar, they produce pathologic effects that vary in character and location. This variance can, in part, be attributed to differences in chemical composition: one is ionic, the other nonionic. Striking pathologic manifestations were reported after high-dose intraventricular administration of both gadolinium compounds, however; indicating that the acute excitatory effects were not agent-specific.

The authors admit that when these drugs are injected intravenously with the typical doses prescribed for conventional MR imaging, it would not be likely that tissue concentrations would produce changes of the severity reported in their study. We should nevertheless be careful with these drugs. A broken blood-brain barrier may allow a drug to reach unusually high concentrations in the cerebral parenchyma; it would be important to know the threshold of accumulation that would allow lesser, but significant, pathologic changes. It is worthwhile to remember that there is always individual variation among tissues and subjects.

There is a tendency for physicians to maximize the amount of, or even overuse, a drug: if a little is good, a lot may be better. The recent protocols for "triple-dose gadolinium" are a good example. While these protocols have not been associated with any higher rate of occurrence of overt neurologic complications, we do not really know about the potential pathologic changes that may be induced from such doses, especially when the blood-brain barrier is broken. Although we radiologists always want to see more, we must remember that there is a risk-benefit ratio to any compound.

There has been the question of injecting gadolinium-based compounds into the intrathecal space for cisternography to diagnose, for example, subtle leakage of cerebrospinal fluid. Other indications for intrathecal and intraventricular gadolinium injection