Other contrast media, not based on gadolinium, have been developed for MRI, but are today not in general use. Superparamagnetic iron particles are selectively taken up following intravenous injection by Kupffer cells, primarily in the liver. Two such iron oxide–based agents were approved in the past: ferumoxides (Endorem, distributed in the U.S. as Feridex, and at one time in use worldwide), with a particle size range of 50 to 180 nm, and Resovist (which was previously available in Europe), with a particle size of ~60 nm. The principal relaxation effect of these large particles was on T2 (due to susceptibility effects, with the contrast agent causing a decrease in signal intensity), with scans performed in a delayed fashion postinjection, allowing time for liver uptake. Resovist was also approved for bolus injection (dynamic imaging), with T1-weighted scans and positive contrast enhancement noted in this application. The safety profile for Feridex was not comparable to that of the gadolinium chelates, with a substantially higher incidence of adverse reactions. The safety profile of Resovist was superior to that of Feridex.

In Fig. 48.1, imaging with Resovist reveals a small hypervascular lesion on Fig. 48.1a, the dynamic scan, with prominent iron uptake on Fig. 48.1b, the delayed scan (white arrow), compatible with an adenoma. In Fig. 48.2, the pre-contrast in-phase T1-weighted scan (Fig. 48.2a) reveals a cirrhotic, nodular liver. On Fig. 48.2b, the delayed post-contrast scan (using Resovist), a subcapsular hepatocellular carcinoma (white arrow) and multiple low signal intensity regenerating liver nodules (black arrows) can be identified. In Fig. 48.3, a delayed post-contrast scan (using Resovist), spread of neoplastic disease to the liver (from a pancreatic primary) is readily identified (white arrow). There is excellent tissue contrast between tumor and normal liver, the latter with uptake of this iron-based agent (and thus low signal intensity on T2-weighted scans). Dynamic post-contrast T1-weighted imaging with a gadolinium chelate in this instance provided poor tumor versus normal liver differentiation (image not shown).
Teslascan, a manganese (Mn)-based agent, was approved in the late 1990s for delayed liver imaging. Unlike the gadolinium chelates, this agent freely dissociated after IV injection, yielding free Mn. Safety concerns led to eventual withdrawal of this agent. Like Feridex, the incidence of adverse events was substantially higher as compared with the Gd chelates. T1-weighted images were employed post-contrast (with Mn having paramagnetic properties similar to Gd, but of lower magnitude).

Oral MR contrast agents are classified according to the observed signal intensity (SI): positive (“bright” lumen), negative (“dark” lumen), or biphasic. Several agents were at one time commercially available in some countries, with generally low utilization. Positive agents originally included dilutions of the gadolinium chelates, specifically formulated for oral use (these are no longer available commercially), and solutions of iron or manganese ions. Some natural substances, such as milk, vegetable oil, green tea, and blueberry juice, and some manufactured products, such as ice cream, also act as positive oral contrast agents, due to either high fat or manganese ion content. Agents containing manganese typically are biphasic in character, with high SI on T1- and low SI on T2-weighted images. Negative contrast agents, which provided a dark lumen on both T1- and T2-weighted images, included several different iron particulate preparations. Water can be used as an oral contrast agent, but its use is limited by intestinal resorption. Barium sulfate can also provide some luminal contrast, with SI (low on T1 and low to high on T2) dependent on administered concentration and subsequent dilution.

![Fig. 48.2](image)

![Fig. 48.3](image)