Hepatic Cryosurgery with Intraoperative US Guidance

An estimated 138,000 new cases of colorectal cancer were diagnosed in the United States in 1995. More than 55,000 people were expected to die of the disease in that year, which made colorectal cancer the third leading cause of cancer deaths in the United States. Over 18,000 new cases of primary malignant liver tumors and biliary tumors were expected for 1995, with over 14,000 deaths (1).

Approximately 10%–20% of patients with primary or metastatic liver tumors are considered to have surgically resectable tumors (2). These two groups (patients with metastatic colorectal malignancies and patients with primary hepatic malignancies) represent the vast majority of patients eligible for resection or ablation of hepatic lesions. A 5-year actuarial survival rate of approximately 33% and a 5-year disease-free survival rate of approximately 22% are expected in patients who successfully undergo hepatic resection (3,4). Because removal or destruction of all malignant foci is the only curative treatment currently available, a technique that would expand the proportion of patients eligible for these therapeutic options would be considered desirable (5,6).

Cryosurgery, the destruction of tumorous tissue in situ by means of freezing, allows physicians to ablate localized areas of tumor-bearing liver (7–10). Cryosurgery is currently used in patients with prostate malignancies, in addition to patients with liver malignancies, and is being examined for use in a wide range of other benign and malignant diseases (11–14). The technique involves the insertion, with ultrasonographic (US) monitoring, of one or more cryoprobes into the surgically exposed liver and subsequent freezing of diseased tissue.

In comparison with conventional segmental or lobar hepatic resection, in which large amounts of normal hepatic parenchyma are removed, cryosurgery is a more focal destructive process that affects only a small amount of normal liver. Therefore, some patients with tumors that cannot be resected with standard surgical techniques may be candidates for tumor ablation with cryosurgery. Some patients who fit this category include those with tumor in multiple lobes or in proximity to major vasculature or patients with underlying liver disease and limited hepatic reserve. This technique essentially extends the indications for surgery to patients whose tumors were previously thought to be unersectable (9,15,16). Long-term results now indicate that survival after cryosurgery is equivalent to survival after hepatic resection but with a lower associated morbidity (17,18).

The benefits of hepatic cryosurgery are potentially maximized through collaboration between surgeons with experience in hepatic surgery and radiologists who are well versed in US. At many medical centers, surgeons have purchased US equipment and perform examinations without consulting radiologists. Given the heavy clinical demands that most surgeons face, it is unlikely that they would have time to gain the depth of experience with US technology and scanning techniques that most radiologists who are experienced with US possess. In addition, owing to the relatively infrequent use of hepatic cryosurgery at most institutions, surgery departments often do not want to spend the large amounts of money that may be necessary for state-of-the-art US equipment with multiple, dedicated probes.

Unfortunately, many radiologists have not enthusiastically embraced the principle of intraoperative US despite the fact that modern hepatic cryosurgery was developed by a radiologist and was first practiced as a collaborative effort between radiologists and surgeons (19). This reluctance may be due to the fear of potentially long absences from the radiology department. In our experience, the average cryosurgery procedure needs the radiologist's involvement for approximately 1 hour, although complicated cases may last several hours. We believe that the effect on the functioning of the radiology department can be minimized by establishing a departmental consensus on the need for radiologic involvement in intraoperative US and for backup coverage by colleagues.

The establishment of rapport with referring surgeons can minimize the time a radiologist must be in attendance by encouraging the surgeon to give prior notice of a scheduled procedure and to call for a radiologist only when scanning is needed. Radiologists and sonographers also need to familiarize themselves with the cases by reviewing relevant images before going to the operating room.

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3 They also need to communicate with the anesthesiologist to minimize the time a radiologist must be present in the operating room.

4 In our experience, ultrasonography is usually not required in the immediate postoperative period.

5 Patients without a malignancy or with nonmalignant liver lesions should be selected to identify the appropriate candidates for surgery.

6 Certain patients with metastatic liver tumors that are scattered in portions of the liver that are not well vascularized may benefit from cryosurgery.

7 Patients with large tumors may benefit from cryosurgery if they are not candidates for surgery.

8 Patients with cirrhosis and patients with operative risk may benefit from cryosurgery.

9 Patients with liver cirrhosis or with progressive liver disease may benefit from cryosurgery.

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From a technical standpoint, there is no limit to the number of lesions that can be treated with cryosurgery. At the University of Wisconsin, however, we use standard surgical criteria for liver resection as a guide to the number of lesions that will be treated. Our current limit is four lesions because patients with larger numbers of lesions have high hepatic and systemic recurrence rates after resection. Other authors have treated more lesions with varying levels of success, although long-term survival data are not yet available (16,22-27).

INDICATIONS

Patients with primary or secondary malignant liver tumors and who are candidates for resection are also generally amenable to cryosurgical ablation. Certain patients are particularly appropriate for cryosurgery: (a) patients with fewer than four lesions that are scattered in multiple segments of the liver, (b) patients with tumor in proximity to major hepatic vasculature where a standard surgical margin would not be possible, and (c) patients with limited hepatic reserve who would be unable to tolerate removal of large amounts of liver tissue (16-19,21).

ROLE OF INTRAOPERATIVE US

Intraoperative US serves two vital functions in the treatment of liver lesions. The initial and most critical role of intraoperative US is to aid decision making at the time of surgery. Intraoperative US has been shown to reveal 7%-35% more lesions than any preoperative imaging technique, including US, computed tomography (CT), magnetic resonance (MR) imaging, and CT during arterial portography (20,25,26,28-30).

At the University of Wisconsin, every hepatic cryoablation or resection is preceded by laparoscopic or open intraoperative US of the liver. On the basis of the location, size, and number of lesions, the decision is made to freeze, resect, or perform a combination of cryosurgery and resection. If the patient is considered incurable by surgical methods owing to the large number of lesions, the abdominal incision is closed, and the patient is referred for palliative therapy.

Intraoperative US plays an important role if the decision is made to freeze or resect. Cryosurgery is not a new surgical method; however, the freezing of tissue has historically been limited by the physician’s inability to monitor the procedure (9,31). One of the main advantages of hepatic cryosurgery compared with other tissue- ablation techniques (radio-frequency ablation, high-intensity focused US, and ethanol injection) is the ease of monitoring needle and probe placement, as well as the precision of monitoring the freezing process, with real-time US guidance (25,32-34). The interface between frozen and unfrozen liver causes an extreme impedance mismatch, which results in a highly echogenic edge with posterior acoustic shadowing (34,35). Therefore, important normal hepatic structures can be avoided because of the highly visible nature of the ice ball at US. The inability of sound to penetrate the ice ball implies that if a lesion is still visible, it has not been adequately treated.

Previous in vivo animal studies (15,34,35) have shown that the area covered by the ice ball seen at US corresponds well to the area of subsequent tissue necrosis. One should be cautious, however, before considering a nonvisible lesion adequately treated. Because it may not be possible to visualize all margins of the ice ball with a single US window, the distal portion of the lesion is at highest risk for an incomplete freeze. Also, the peripheral margins of the cryolesion are the farthest areas from the cryoprobe and are therefore the most likely areas to be exposed to nonlethal temperatures. This can be a particular problem when an adjacent blood vessel causes a defect in the ice ball, which could contribute to nonfreezing of tumor.

US EQUIPMENT

At our center, a US unit (SSD-2000; Aloka Ultrasound, Wallingford, Conn)
with dedicated intraoperative probes is used for cryosurgical cases. Intraoperative probes generally are high-frequency, linear-array (5.0–7.5-MHz) probes with a unique geometry that allows them to fit into small body cavities. We specifically favor T-shaped linear, finetip curvilinear, and biplane transrectal linear transducers.

Probes should be side firing so that they can be held in the flat of the hand while scanning the liver surface (20,33,34). This is particularly important for lesions located near the dome of the liver, because there is minimal space between the liver and the diaphragm for the US probe and the examiner’s hand. Most convex-array probes designed for general external US will not provide satisfactory resolution or will not fit over the dome of the liver or under the liver surface.

Dual, orthogonal plane imaging is essential for placement of cryoprobes in the center of the mass. After placement of the needle into the mass with US guidance with a longitudinal transducer, the probe can be turned 90° relative to the path of the needle to confirm that the needle (or wire or cryoprobe) is placed in the center of the mass. This can also be accomplished by using two transducers that are oriented in different 90° planes or by using a single biplane transducer.

It may not be possible to turn the transducer 90° in many tight locations because of the position of the transducer cord. For this reason, some authors (20,36) favor the use of a biplane transrectal transducer. The needle can be placed into the lesion by using the longitudinally oriented crystal for US guidance, and the axial crystal can be used to confirm placement in the center of the lesion. Failure to check the position of the needle in the axial plane may result in a cryoprobe with an eccentric placement in relation to the mass. This could lead to an asymmetric ice ball, which may produce nonlethal temperatures at the periphery of the ice ball.

**CRYOSURGERY EQUIPMENT**

A supercooled liquid nitrogen system (Accuprobe 450 SP; Cryomedical Sciences, Rockford, Md) pressurized with nitrogen gas is used for cryosurgery at our center. (Another liquid-nitrogen-based cryosurgery system is the Cryotech unit [Candela Laser, Wayland, Mass.]) Liquid nitrogen is circulated from a lower, or source, dewar flask through the probe ports and into an upper, or return, dewar flask. Up to five ports can be used at one time. Active thawing is achieved with circulation of warm nitrogen gas.

Probes can be set to achieve a target temperature or be programmed to pulse liquid nitrogen at 25%, 50%, 75%, or 100% flow. The operation of a probe at a percentage of full capacity results in an ice ball that is less than maximum size. Probe temperature in this case is only a few degrees warmer than that of probes operating at 100% flow. This feature is particularly useful when creating ice balls in proximity to areas in danger of inadvertent freezing, such as the bile ducts. Monitoring of the probe-tip temperature is facilitated with a computer screen located on the front of the console.

In the event that the source dewar flask is emptied before the procedure is complete, supply levels can be regenerated by transferring the contents of the return dewar flask back to the supply flask. The probes may remain in place during this procedure.

A new class of devices (7,37) has recently been introduced (Cryo-Clip; Cryomedical Sciences, Rockford, Md) and relies on a gas (the Joule-Thomson effect) in the tip of the device to capture the argon gas and use it as a refrigerant for cooling tissue. Preliminary preliminary findings suggest that this may improve desiccation of cancer cells. The clinical findings await further trials.

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**Figure 2.** Liver metastases from uterine sarcoma in a 68-year-old woman. The large lesion in the right lobe was surgically resected. (a) Contrast-enhanced CT scan shows an additional lesion (arrow) in the left lobe adjacent to a hepatic vein branch. The CT scan is indeterminate for simple cyst versus small metastasis. (b) Intraoperative US image shows the smaller lesion (arrow) to be a solid mass. The proximity of the lesion to the left hepatic vein, in addition to the patient’s limited hepatic reserve after excision of the right lobe, makes cryosurgery the only viable option for curative treatment. (c) Cryoprobe insertion is demonstrated in an animal model. An 18-gauge, diamond-tipped needle with a Teflon-coated hub has been inserted in the lesion. The needle has been removed, and a J wire (arrow) with a 0.035-inch (0.875-mm) diameter has been inserted in the hub. A dilator (d) with a diameter of 8 mm and sheath (e) are advanced over the J wire. (d) Intraoperative US image shows the advance through the sheath of the hyperechoic cryoprobe (open arrows) after removal of the wire and dilator. The tip of the cryoprobe is in the lesion (solid arrow). (e) Intraoperative US image shows the ice ball, which is defined by the hyperechoic rim and posterior acoustic shadowing. As the ice ball grows, it begins to wrap around the adjacent vessel. A continuous inflow of warm blood protects the vessel from damage.

**Figure 3.** Multiplanar oblique coronal and sagittal views demonstrating normal hepatic parenchyma adjacent to the intrahepatic bile ducts in a 23-year-old man. A peripheral, minimally calcified, but otherwise normal right hepatic lobe is demonstrated. A transhepatic cholangiogram (not shown) confirmed the absence of ductal obstruction. A normal right lobe was left to maintain the patient’s hepatic reserve. A new class of devices (7,37) has recently been introduced (Cryo-Clip; Cryomedical Sciences, Rockford, Md) and relies on a gas (the Joule-Thomson effect) in the tip of the device to capture the argon gas and use it as a refrigerant for cooling tissue. Preliminary findings suggest that this may improve desiccation of cancer cells. The clinical findings await further trials.

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**Figure 4.** Demonstration of cryoprobe placement within the hepatic vein and the hepatic parenchyma using a combination of orthogonal plane US and intravascular US imaging. The cryoprobe (B) is seen to bridge the hepatic parenchyma and the hepatic vein (A). Below, a 10- to 20-mm-diameter transverse image of the cryoprobe is obtained using orthogonal plane imaging. A transparent plastic sheath (D) with a 15-mm-diameter center lumen is placed over the cryoprobe. The cryoprobe is then advanced through the hepatic parenchyma, and the tip of the cryoprobe is advanced through the hepatic vein. A new class of devices (7,37) has recently been introduced (Cryo-Clip; Cryomedical Sciences, Rockford, Md) and relies on a gas (the Joule-Thomson effect) in the tip of the device to capture the argon gas and use it as a refrigerant for cooling tissue. Preliminary findings suggest that this may improve desiccation of cancer cells. The clinical findings await further trials.

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Figure 3. Multiple lesions from metastatic leiomyosarcoma in a 34-year-old patient. (a) On a CT scan, the largest lesion is seen posteriorly, adjacent to the inferior vena cava. The location of this lesion immediately adjacent to the inferior vena cava makes this tumor unresectable with conventional surgery. (b) Contrast-enhanced CT scan obtained 3 years after cryosurgery shows only a residual cyst in the region previously occupied by tumor. (c) CT scan obtained 5 years after cryosurgery shows the lesion is completely resolved. This case demonstrates the ability to treat successfully with cryosurgery lesions in direct contact with major vascular structures.

Figure 4. Demonstration in an animal model of the ability to ablate cryosurgically all hepatic parenchyma up to major vascular structures. (a) Photomicrograph of a longitudinal section of the hepatic vein shows necrotic parenchyma (N) extending to adventitia (arrows). Intact hepatic parenchyma (L) is present beyond the cryolesion. (Hematoxylin-eosin stain; original magnification, ×200.) (b) Higher-power photomicrograph shows the wall of the hepatic vein with a clear line of demarcation (arrows) between adjacent necrotic (N) and intact (L) hepatic parenchyma. Note complete necrosis of hepatic parenchyma adjacent to the hepatic vein (arrowheads). (Hematoxylin-eosin stain; original magnification, ×100.)

A new class of cryosurgical device has recently become available. This system (Cryocare; EndoCare, Irvine, Calif) uses argon gas as the coolant and relies on the rapid expansion of gas (the Joule-Thomson principle) in the tip of the cryoprobe to cool tissue rapidly. Differences between the argon gas system and devices that use liquid nitrogen include no bulky insulation on cryoprobes, faster freezing rates, and no requirement for large, heavy dewar flasks in the argon gas unit. Results of preliminary in vivo studies (37) suggest that rapid cooling of tissue may improve destruction of malignant cells. The clinical implications of this finding await the results of clinical trials.

The probes used to freeze deep hepatic lesions are blunt-tipped, disposable cryoprobes with an outer diameter of 3 or 8 mm. These probes produce ellipsoid ice balls with a maximal diameter of approximately 3 or 5 cm, respectively. It should be noted that, in situ, ice-ball size is variable and depends on the local thermal environment and on the proximity to major vessels. The apex of the ice ball extends less than 1 cm beyond the tip of the probe; therefore, when the probe is placed, the end of the probe defines the distal margin of the freeze zone.

Flat and paddle-shaped probes can be used for freezing of surface lesions. However, cracking of frozen hepatic tissue during thawing is a serious complication that can cause massive hemorrhage (20,38). For this reason, we preferentially resect surface lesions when possible.

MECHANISM OF LIVER DAMAGE CAUSED BY FREEZING

The mechanism for destruction of hepatic tissue by means of freezing depends on the location of tissue in relation to the cryoprobe. In areas close to the cryoprobe, temperatures rapidly approach −190°C, causing ice crystals to form within and around cells. Subsequent rupture of the cell membrane during thaw and rehydration results in tissue death. Farther away from the probe, where temperatures drop more slowly, ice forms within venules and arterioles because cell walls impede intracellular ice crystal formation. Solutes are excluded from the forming ice, making extracellular fluid hypertonic. Unfrozen parenchymal cells will dehydrate to equilibrate the resultant chemical gradient, which causes expansion of blood vessels that then rupture during thawing. The resulting short-term hypoxia contributes to the death of surviving cells. Therefore, cell death within the freeze zone is due to a combination of intra- and extracellular ice crystal formation, cellular dehydration and rupture, and hypoxia from small vessel destruction (Fig 1) (39-41).

TECHNIQUE

After the liver has been exposed and the lesions have been located with intraoperative US, one or more cryoprobes are inserted into or around the lesion. Probe placement is designed to create an ice ball that will encompass the lesion and a 1-cm mar-
gin of normal hepatic tissue. The ideal path for the insertion of the probe traverses some normal liver to aid in hemostasis after freezing is completed and the probes are removed. The path of the probe is also designed to avoid major vessels and bile ducts (23).

The cryoprobe is inserted by using a coaxial guidance system (Onik Percutaneous Access Kit; Cook, Spencer, Ind). An 18-gauge, Teflon-coated, diamond-shaped needle and hub are inserted through the lesion with US guidance to approximately 1 cm beyond the distal margin (Fig 2). Needle position should be confirmed with US in two orthogonal planes and repositioning performed as needed. The stylet is then removed, and a 0.035 inch [0.875 mm] in diameter) with a stiff mandril proximal to a "J" end is inserted into the hub. The stiff end of the wire allows more secure anchoring in liver tissue than is possible with conventional J wires. The wire should be visualized with US to ensure that it is completely out of the hub and within hepatic parenchyma. This provides stability for placement of the dilator, sheath, and probe while the original track defined by the initial needle placement is maintained. The needle hub is then removed over the wire, and the dilator and sheath are advanced into the liver over the J wire. Because the sheath tip begins approximately 1 cm from the tip of the dilator, it is important to advance the sheath approximately 1 cm once the tip of the dilator is in satisfactory position. Finally, the wire and dilator are removed, and the probe is inserted through the sheath with US guidance. For freezing, the sheath is pulled back to expose the freeze zone of the probe.

Once the probe is in position, it is anchored in place by rapidly lowering the probe to approximately -100°C. The target tissue is then frozen, with US control, by varying the amount of flow through individual probes. When an ideal ice-ball size is obtained, the flow rate is decreased to 50% to prevent further expansion of the ice ball and to conserve nitrogen.

The ice ball is markedly hyperechoic with posterior acoustic shadowing, which allows accurate monitoring of the progression of the freeze zone (Fig 1e). Monitoring of the freeze may require viewing the ice ball from several different perspectives—from directly on top of the ice ball to the undersurface of the liver. The transducer should never be allowed to freeze to the developing ice ball because this will damage transducer elements.

Most centers perform a double freeze-thaw cryosurgical cycle. The authors of early animal studies (31,32,42) suggested that multiple freeze-thaw cycles may be necessary for complete tissue necrosis. This technique was contraindicated in patients with a history of hepatic cirrhosis or a second freeze-thaw cycle could be considered. This took advantage of vessels in the periphery of the lesion, which were more likely to be necrotic (40).

Experiments in this laboratory (43,44) suggested that a single freeze-thaw cycle followed by a second freeze-thaw cycle would have a role in the treatment of liver tumor. Studies in this laboratory (15,26) showed that the same outcome could be obtained in a single freeze by the addition of a second freeze-thaw cycle. This modification has the advantage of eliminating the freeze-thaw cycle after the initial freeze-thaw cycle, which was generated by predetermined cycle times.
freeze-thaw cycles were necessary for complete tissue destruction. The first freeze was thought to cause cell destruction close to the probe tip where lethal temperatures below −20°C could be consistently achieved. The second freeze enabled more distal areas also to become completely ablated. This may be due to destruction of vessels in the margin of the cryolesion, which leads to hypoxia and cell death in the hours after the freeze (40).

Experimental and clinical evidence (43,44) suggest that a double freeze-thaw cycle may increase the amount of hepatocellular injury, which plays a role in thrombocytopenia, myoglobinuria, and multisystem organ failure (16,26,43,45). Because of this complication, a modified double freeze-thaw cycle is now used at many centers. This modified double freeze-thaw cycle incorporates only a partial thaw after the first freeze and is better tolerated by patients.

Serum aspartate transaminase levels on postoperative day 1 appear to correlate with the development of thrombocytopenia, which peaks on postoperative day 3 (45). Patients considered at high risk for postoperative thrombocytopenia due to a large-volume freeze or a double freeze-thaw cycle can be monitored with serial measurements of aspartate transaminase levels.

As expected, aspartate transaminase levels have been found to be statistically significantly higher in patients who underwent double freeze-thaw cycles than in those who underwent single freezes.

Peripheral Lesions

Probe placement in spherical lesions located distant from major vessels and bile ducts is relatively straightforward. As in surgical resection, successful cryoablation necessitates destruction of the tumor in addition to a 1-cm surgical margin (46). The probe is placed through the center of the lesion, with the distal end of the probe defining the far freeze-zone margin.

Central Lesions Near Major Blood Vessels

The fccal nature of cryosurgery makes it feasible to ablate lesions located near major vessels, where a conventional surgical margin may not be possible (Fig 3). It is possible to create an ice ball immediately adjacent to a vessel wall; a “heat-sink” effect, created by warm, flowing blood, prevents damage to the vessel endothelium (Fig 4) (23,47). In fact, one or more probes can be used to create an ice ball that wraps around a vessel (Fig 2e). The ice ball will not expand symmetrically owing to the heat-sink effect of the adjacent vessel (34), which potentially necessitates a probe with a larger diameter or a greater number of probes. Probes should also be placed asymmetrically in or around the lesion, with the probes placed closer to the vessel than would be necessary for a peripheral parenchymal lesion (Fig 5).

Large Lesions and Asymmetric Lesions

The maximum ice-ball size for a single-probe freeze is determined by means of probe size, percentage of maximum cooling selected, local thermal environment, and probe performance. For larger or nonspherical lesions, it can be difficult to encompass the entire lesion in addition to a 1-cm margin of surrounding normal tissue by using only one probe to create the ice ball. Therefore, multiple probes may be needed to destroy lesions that are larger than the maximum ice-ball-creation capacity of a single probe (Fig 6).

Decisions about the maximum-sized lesion that can be frozen should be made on a case-by-case basis and should take into account the increased potential for complications with larger-volume freezes, the increased surgery time, and the biologic characteristics of the particular disease being treated.

Complicated, three-dimensional ice-ball shapes can also be achieved by using multiple probes (16,24). Continuous US monitoring is particularly important in this situation to ensure complete coverage of the tumor with the ice ball and to avoid unnecessary
damage to normal liver because multiple probes can act synergistically to produce an unexpectedly large ice ball. If a lesion does not appear to be adequately covered by the ice ball, additional probes should be inserted as soon as possible.

Unlike in prostate cryosurgery, thermocouples are not routinely used for temperature monitoring in hepatic cryosurgery. However, thermocouples may prove useful when it is difficult to obtain a 1-cm freeze margin owing to the proximity of vital structures such as bile ducts. Alternatively, needles may be placed around the periphery of the lesion or in difficult-to-monitor areas to ensure adequate coverage by the ice ball. By freezing these needles in place, one can ensure that the ice ball at least attains coverage of a portion of the needle track.

**COMPLICATIONS**

Frozen hepatic tissue is predisposed to hemorrhage when the tissue cracks during the thawing process. When freezing a deep lesion, the ice ball is surrounded by normal hepatic parenchyma, which aids hemostasis by tamponading bleeding tissue. At the University of Wisconsin, we place a roll of cellulose-based surgical fabric (Surgicel; Johnson and Johnson, Arlington, Tex) into the cryoprobe track either directly or by using the sheath-dilator system as a plunger as soon as the thawing process allows the cryoprobe to be extracted. Generally, no other intervention is needed (38).

Freezing of superficial lesions or inadvertent freezing of the liver surface is somewhat more of a problem. Extension of the ice ball to the liver surface predisposes the capsule to cracking and potentially leads to severe hemorrhage. Because this complication, wedge resection should be considered in cases of shallow or surface lesions. In general, bleeding should be controlled with packing, use of clotting agents, pressure, or oversewing of the cracked area. Segmental resection was reported (9) necessary in a case of massive hemorrhage. In one large series (26), repeated surgery because of bleeding was necessary in 12 of 140 (8.6%) patients.

Delayed bleeding is an infrequent but important complication seen in fewer than 1% of patients (48). This complication may be due to thrombocytopenia seen in patients who have undergone a large-volume freeze at cryosurgery (45). Although infrequent, this complication is a known source of mortality and should play a role in patient selection.

Clinical hypothermia is a potential complication in cryosurgical cases. The use of a warming device that regulates patient temperature by circulating warm air around the patient's body, in conjunction with conventional temperature-regulation techniques such as heating fluids and inhaled gases, substantially decreases the occurrence of hypothermia (26, 27, 49).

Acute myoglobinuria after hepatic cryosurgery has also been reported (26) in virtually all cases. In most cases, myoglobinuria is limited to 1-3 days after the procedure. In severe cases, myoglobinuria can result in acute tubular necrosis and impaired renal function. Renal compromise due to myoglobinuria appears to be directly related to the volume of tissue frozen; therefore, renal function should be considered before freezing large tumors. In all cases (particularly if myoglobinuria becomes severe after cryosurgery), urine flow should be closely monitored and maintained with the use of hydration and diuretics, and consideration should be given to alkalizing the urine (16, 26).

Biliary or vascular fistula is an additional risk. Ducts and small vessels are not protected by the heat-sink effect and are at risk for injury during the freezing, reporting, or control phases of the procedure. Use of the biopsy needle or stent-protected sheath-needle during cryosurgery may help prevent the occurrence of these complications. Several criteria are used to monitor complications, which include the presence of fever, changes in laboratory values, or the development of a thermal burn at the site of cryotherapy (23).

**Figure 8.** Regression of the cryolesion in a completely frozen colon cancer metastasis in a 51-year-old man who underwent resection of the left lobe and freezing of one metastasis. (a) Contrast-enhanced CT scan obtained 1 month postoperatively shows the cryolesion. No solid mass is seen on any section. (b) Contrast-enhanced CT scan obtained 4 months postoperatively illustrates the shrinking cryolesion. The necrotic tissue is slowly being resorbed.

### Patient Survival after Hepatic Cryosurgery

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Note: ND = no data.
* Number is mean follow-up.
† Data are for hepatocellular carcinoma larger than 5 cm in diameter.
‡ Data are for hepatocellular carcinoma 3 cm in diameter or smaller.

**POSTOPERATIVE MANAGEMENT**

One of the most commonly observed complications is the adrenal gland. As a rule, patients are not operated on with an adrenal and as such, the adrenal gland may be at risk for hemorrhage. In most cases, this complication is limited to a 2-week period (20) and is usually of no significance. The patient usually experiences no symptoms and the adrenal gland heals without sequelae in the majority of cases (20). However, in some cases, severe hemorrhage may occur (20). The presence of an adrenal gland may be of benefit in the event of a complication. The authors have observed that the adrenal gland can be used to control bleeding in areas adjacent to the tumor.

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and are easily damaged by the advancing ice ball (47). A 6% prevalence of injury to major bile ducts has been reported (26). The path of the cryoprobe must be designed to avoid these structures, and shielding of the porta hepatis can be performed by placing an insulating barrier between the expected position of the ice ball and the bile ducts (Fig 7).

For lesions adjacent to the major hepatic ducts, a bile duct warmer or warm saline infused into the ducts can be used as an additional safety device. If a major bile duct is injured and stenosis subsequently occurs, stent placement has been shown to be adequate treatment (26). Most biliary injuries can be managed conservatively, but if they begin to cause symptoms or become infected, percutaneous drainage may be necessary (16). Liver abscesses that develop in the cryolesion are infrequent and should be drained percutaneously.

Several other common and uncommon complications have been encountered with hepatic cryosurgery. These include fever (common), right pleural effusion and atelectasis (common), thermal injury to adjacent organs (uncommon), bile duct fistulas (uncommon), and liver failure (uncommon) (23,26).

ADVANCES IN CRYOSURGERY

Some centers have started to perform percutaneous or laparoscopically guided hepatic cryosurgery. These methods could potentially make hepatic cryosurgery even less invasive with the elimination of a major abdominal incision. We believe, however, that intraoperative US is crucial to appropriate patient triage and to the technical success of the cryosurgery owing to the large number of tumors that are not visualized with any preoperative imaging modality. A purely percutaneous procedure performed without intraoperative US, while technically feasible, does not take advantage of the unparalleled imaging capabilities of a US transducer placed on the liver surface and is therefore almost certain to miss a substantial amount of tumor. Failure to use intraoperative US may lead to either over- or undertreatment of patients at a time that is the sole window for curative treatment.

CONCLUSION

Cryosurgery of the liver has proved to be a valuable tool in combating metastatic disease in the liver. To date, survival rates for patients treated with cryosurgery are comparable to those achieved with conventional hepatic resection, but with less associated morbidity (Table 15,20). In addition, use of the technique expands the scope of treatable disease by increasing the number of patients eligible for surgery (23–27).

In combination with intraoperative US monitoring, cryosurgery allows specific targeting of diseased tissue with minimal damage to uninvolved liver parenchyma. These advantages have made hepatic cryosurgery a standard treatment for malignant liver disease at many medical centers. Continued technological advances related to laparoscopic surgery, cryoprobe design, and imaging guidance with modalities such as CT and MR imaging should make this technique even more effective and less invasive in the future.

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