

The background of the page is a light blue-grey color with a subtle grid pattern. Overlaid on this grid are numerous small, square images of tissue blocks, some showing dark, irregular shapes (likely tumors) and others showing more uniform, lighter-colored tissue. These images are arranged in a way that suggests a large-scale study or a collection of samples.

# Feature

## Who Owns Diagnostic Tissue Blocks?

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**T**he question of ownership of human tissues has generated debate for centuries.<sup>1,2</sup> In the last 20 years, the attention of academicians in bioethics and law, as well as the lay press, has focused on ownership of tissues collected specifically for research purposes.<sup>2-5</sup> Ownership of tissues originally collected for diagnostic purposes, and now residing as formalin-fixed, paraffin-embedded tissue blocks within pathology laboratories throughout this country, has not received as much attention. Who owns these tissue blocks?

When patients have tissue excised at a hospital or outpatient surgery center, this tissue is sent to a hospital pathology department or independent pathology laboratory for processing, histologic examination, and diagnosis. Following diagnosis, these paraffin blocks are kept in department storage. State laws determine the legal conditions under which these blocks are maintained, and professional organizations (including the Joint Commission of Accreditation of Health Care Organizations and the College of American Pathologists) also have their own guidelines and recommendations.<sup>6</sup> Prolonged storage ensures that tissues are available for future study, should new testing or treatments germane to the patient's disease be developed. Additionally, this mandatory storage facilitates outside slide consultations, in case the patient seeks a second opinion elsewhere, and may be required for medical-legal cases. If pathology departments decide to retain tissue blocks beyond the mandatory limits, state law may require they continue to abide by all the regulations for tissue block storage.<sup>6</sup>

### Legal Caretakers of Tissue Blocks

Pathology departments are recognized as the legal caretakers of diagnostic paraffin blocks.<sup>6</sup> Guardianship is a serious responsibility that must be attended to carefully. Blocks should be tracked appropriately, be readily retrievable, and all reasonable efforts should be made to retain diagnostic tissues within the blocks (ie, not "exhaust" the block). It is advisable the original pathology department retains control of diagnostic paraffin blocks; tissues are considered to be part of the medical record

and institutions legally are required to keep comprehensive medical records. Recut slides and unstained slides for special tests satisfy most patient requests for outside consultations; in rare cases (usually medicolegal), courts may order the transfer of original materials to another site. If blocks must be moved outside the original facility, departments should carefully document their movement, including receipt of all materials by the recipients, and date and condition of return of the materials.<sup>7,6</sup> Depending on the situation, departments may be required to have a signed HIPAA release from the patient prior to sending materials to another institution or laboratory. If the patient requests slides or blocks to be transferred elsewhere for a research study (not related to clinical treatment for the patient), consultation with the caretaker institution's legal department may be helpful.

### Ownership of Excised Tissue

While pathology departments are the recognized legal guardians, state and federal laws do not address specifically the issue of ownership of excised tissues.<sup>8-10</sup> "Ownership" of excised human tissues remains a debated and confusing topic among physicians, bioethicists, legal experts, and average citizens.<sup>1-3,4,5,9,11-13</sup> Individual pathologists often consider patients to be the owners of their excised tissues and thus make efforts to accommodate patients' instructions.<sup>14</sup> Hospitals and pathologist organizations, in contrast, may consider diagnostic tissues, blocks, and slides to be the property of the original pathology department<sup>7,8</sup>; this may reflect interest in ensuring compliance with applicable laws and protecting physician rights in medical-legal cases. In practice, there are no specific laws, case law, or prior legal rulings that explicitly address ownership of diagnostic materials.<sup>8-10</sup> Prior court rulings suggest individuals may retain some property rights (and thus "ownership") of certain tissues, especially concerning embryos, ova, sperm, and donor organs for transplantation.<sup>2,13</sup> This distinction—ownership versus guardianship—is critical since, legally, the notion of "ownership" includes the concept of property rights, which may include the right to control property, products derived from the property, or control profits derived from the property.



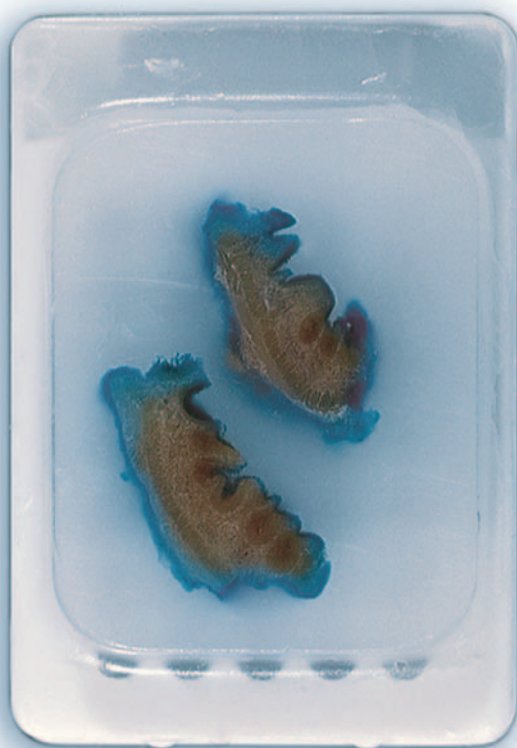
## Tissue and Research

Tissues in diagnostic blocks can be associated with clinical data, including response to treatment, clinical outcome, and diagnosis. As such, diagnostic tissue blocks offer a unique, critical, and valuable resource for translational and clinical research, including biomarker evaluation and drug-development studies. Tissue microarrays constructed from diagnostic blocks have proven to be an invaluable resource for cancer researchers, since this technology permits simultaneous evaluation of hundreds or thousands of tumor samples.<sup>15</sup> As caretakers of tissue blocks, departments determine if these materials are used for research, teaching, or ancillary departmental needs (such as acting as positive controls for special studies).

In legal disputes concerning the research use of excised tissues, courts consistently have rejected the idea that patients are the owners of their excised tissues or retain any property rights. While only three cases have been adjudicated to date, the findings (in both state and federal courts) have been consistent: patients do not have individual ownership, retain property rights, or have complete control over research use of their excised tissues.<sup>9,13</sup> These three cases involved tissues taken specifically for research, so they are not completely analogous to tissue blocks originally taken as part of routine diagnostic protocols. However, in the absence of specific laws or prior case law regarding the use of diagnostic tissue blocks in research, these rulings do offer some interesting and important legal insights.

The first two cases involved disputes over valuable products developed from human tissues. In *Moore vs. the Regents of the University of California*,<sup>16</sup> a physician created and patented a valuable cell line derived from Mr. Moore's tissues, without the patient's knowledge. When Mr. Moore discovered the cell line, he sued to recover a portion of the profits and sued the physician for breaching his fiduciary responsibilities.<sup>12,24</sup> In *Greenberg vs. Miami Children's Hospital Research Institute*,<sup>17</sup> parents of children with Canavan disease (an inherited, rapidly fatal disease) voluntarily provided tissues from affected and unaffected family members, family histories, and funds to a researcher to develop a prenatal test. The researcher succeeded. His university patented the test, charged a royalty fee, and placed restrictions on testing by outside laboratories. The Canavan disease group had intended this to be a free, readily available test; they sued for lack of informed consent, fraudulent concealment of the patent, and unjust enrichment.<sup>4,18</sup> In both cases, the courts denied the patients' property claims and concluded the researcher changed and gave unique value to the original cells, and thus the patient could not profit from the patent.<sup>2,4,9,12</sup> Further, in *Greenberg*, the court ruled that any property rights the patients may have had in the tissues were surrendered at the time of donation.<sup>9</sup>

The third case, *Catalona vs. Washington University*,<sup>19-20</sup> involved a dispute over pure tissue samples. Dr. William Catalona, well known for recognizing the value of PSA screening,<sup>21</sup> established a prostate cancer tissue bank at Washington University (WU). The biorepository eventually held thousands of tissue samples and hundreds of thousands of blood samples, including samples from patients of other WU surgeons. Dr. Catalona decided to move to Northwestern University and wanted to relocate the biorepository there. He sent his patients a form to sign allowing relocation of their samples, and approximately 6,000 patients complied. Washington University refused to move the samples and sued to establish ownership. At trial, patients argued they retained the right to control their tissues, since the informed consent documents gave them the



right to withdraw from the research (and some forms included the right to request sample destruction). Furthermore, patients stated their trust in Dr. Catalona was critical to their consent to donate, since they understood their tissues would be used at his direction. The university countered that the biorepository was an institutional collection, since it contained tissue samples from other surgeons' patients, since WU had provided space and funds for its maintenance, and since WU had paid Dr. Catalona's salary.<sup>2,4,5,13,22,23</sup> The court ruled that WU—not the patients or Dr. Catalona—owned the tissues, and the patients could not force transfer of the samples to another institution. If patients chose to withdraw their consent for the research, the court indicated that federal and state rules gave the university the right to destroy, anonymize, or continue to store (without using them in research) samples.<sup>5,13,22,23</sup>

In all three cases, the courts expressed concern that biomedical research cannot be performed successfully or efficiently if patients can control how their tissues are used in research, how products from their tissues are used, or how profits from products derived from their tissues are shared.<sup>2,9,12,13,22,23</sup> Again, these cases have only adjudicated disputes involving tissues designated for research purposes and have not considered the situation of research on tissue blocks originally taken for diagnostic purposes. However, based on the prior cases, it would appear that as long as departments fulfill their caretaker roles for tissue blocks and follow federal and institutional human subject research regulations, courts would support research on tissue blocks in pursuit of broader biomedical research initiatives. In the absence of specific laws or prior case law, it remains unclear if patients have the right to refuse use of their diagnostic tissue blocks for research.





## The Role of Institutional Review Boards

All research projects meeting federal criteria for human-subjects research must be reviewed prospectively by Institutional Review Boards (IRBs); these internal institutional committees interpret federal guidelines and apply them to submitted research proposals to ensure compliance with federal research regulations. Federal policies on human research are codified in the Code of Federal Regulations (45 CFR part 46, Subpart A—also known as the “Common Rule”) and in the Health Insurance Portability and Accountability Act of 1996. Technically, only research that is federally funded or conducted by federal agencies must meet the Common Rule guidelines. In practice, many institutions require all research proposals to meet these criteria.<sup>10</sup> Importantly, state or local laws governing human-subjects research that otherwise apply or that provide additional patient protection are not affected by these federal laws.<sup>10</sup> The IRB will determine if informed consent is required for the research proposal. Federal research regulations allow excised tissues to be used in research without patient consent, as long as an individual patient’s identity is unknown (anonymous tissue samples) or adequately protected,<sup>9,10,13</sup> though what constitutes adequate protection is not detailed.

In the past, there has been some uncertainty within the research community concerning whether research on diagnostic tissue specimens requires IRB approval and, if so, the type of review required.<sup>9</sup> This uncertainty may reflect the unique bioethical niche these specimens occupy. Diagnostic tissue samples are removed from patients during the course of routine and necessary diagnosis and treatment. As such, some bioethicists consider diagnostic tissues to be “abandoned” by patients, in sharp contrast to tissue samples prospectively collected for research or research biorepositories.<sup>2</sup>

Pathology departments should require IRB approval, IRB exemption, or a letter from the IRB stating IRB approval is not required prior to distributing blocks or sections from diagnostic tissue blocks for research. This protects both potential research subjects and the department. If informed consent is required, departments may want a copy of the signed informed consent form along with the request for the tissues to keep on file.

Pathology department leadership may consider establishing policies regarding disbursement of tissues to outside researchers. Since these policies may affect other clinicians and researchers at the institution, involvement of institutional leaders in this process may be prudent. State laws governing individual patient privacy, genetic testing, and human-subjects research have resulted in important and significant differences in regulations regarding the collection, storage, and use of human tissues in research between even neighboring states.<sup>10</sup> Consultation with the institutional legal department thus may be advisable as well. Since individual IRBs may interpret federal guidelines for human-subjects research differently, internal institutional IRB approval may be appropriate for any outside requests for tissues, even if the requestors have approval from their own IRBs. Above all, as the legal caretakers of these materials, pathology departments should ensure that adequate diagnostic tissue remains in storage for future testing, second opinions, or medical-legal cases.

## Conclusion

In summary, diagnostic formalin-fixed, paraffin-embedded tissue blocks are stored by pathology departments. Pathology departments are the recognized legal caretakers of these tissues and, as such, must abide by hospital, state, and federal regulations. There are no specific state or federal rules regarding ownership of diagnostic tissue blocks. Departments must follow state laws governing the length of storage (typically years) and retrieval of materials and should ensure diagnostic tissue remains in the event future testing, outside consultation, or medical-legal cases require it. Unlike samples specifically collected for research, these diagnostic tissue blocks occupy a unique bioethical niche. These blocks may have research value, especially for clinical and translational research, since they can be linked to information on diagnosis, treatment response, and disease outcome contained within pathology and hospital databases. There are no prohibitions on the use of these tissues in biomedical research, assuming departments follow State laws regarding maintenance of these blocks, ensure diagnostic tissues remain available, and abide by Federal research regulations. In cases involving only tissues originally designated for research use, courts have not found that patients retain ownership or property rights in their excised tissues. Currently, it is not clear if patients have the legal right to prohibit use of their diagnostic tissue blocks in research. Decisions regarding the appropriate use of these materials should be determined by pathology department leadership, in conjunction with institutional leaders, the IRB, and legal counsel, as needed. LM

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