Hibernomas, were first reported in 1906 by Merkel. They are rare benign adipocytic tumors composed in part of brown fat cells with granular, multivacuolated cytoplasm admixed in variable proportion with white adipose tissue.

**Note**

Brown adipose tissue is rich in glycogen, cholesterol and phospholipids. In contrast to white adipose tissue, which stores energy, brown fat is involved in nonshivering thermogenesis. This ability is dependent on the expression of uncoupling protein 1 (UCP1), a mitochondrial proton transporter that uncouples electron transport from ATP production. In humans, brown adipose tissue typically accumulates within the neck, axillae, back, subpleural regions, mediastinum, abdomen and thigh, and is more profuse in the fetus and neonate, in whom it constitutes approximately 5% of body weight. Beginning at about 8 weeks after birth brown adipose tissue gradually decreases. In adult life, it progressively disappears and is confined to the more central parts of the body, which leads to a vest-like arrangement with the greatest yields of brown fat in perirenal, posterior cervical and axillary lymph nodes, and intercostals areas.

**Epidemiology**

Hibernomas account for 1.6% of benign lipomatous tumors and approximately 1.1% of all adipocytic tumors. They are more common (approximately 60%) in the third and fourth decades of life; only 5% occur in children and teenagers.

**Clinics**

The most common site is the thigh followed by the shoulder, back, head and neck, mediastinum and retroperitoneum. Multiple and bilateral hibernomas have also been reported. Hibernomas are usually asymptomatic; clinical symptoms occur from pressure effect on adjacent structures. The majority present as firm, slow-growing, progressively enlarging, painless masses that lie in subcutaneous tissue; at least 10% are intramuscular. Occasionally, they are rapid growing and infiltrating adjacent structures.

**Imaging**

-Radiography: May show a faint soft tissue mass or swelling, without areas of calcification or bony erosion.

-Sonography: Ultrasoundography shows a well-circumscribed uniformly hyperechoic mass (figure 1). Color doppler sonography usually shows hypervascularization with enlarged vessels (figure 2).
Figure 1. Ultrasonography shows a circumscribed hyperechoic mass at the neck. Biopsy showed hibernoma. Figure 2. Color Doppler sonography shows hypervascularization of the lesion.
**Computed tomography:** Usually shows a lobulated, well-circumscribed mass with multiple septations and variable contrast enhancement. An incomplete, thick, solid-appearing wall is usually present.

**MR imaging:** Shows a well-circumscribed and encapsulated mass whose signal intensity is intermediate between subcutaneous fat and muscle; the lesion is isointense or relative hypointense compared to subcutaneous fat and hyperintense compared to muscle, with contrast enhancement and linear septations (figure 3). Diffuse enhancement is usually observed following gadolinium administration. There may be incomplete fat suppression because of the nature and amount of lipids.

**Scintigraphy:** Bone scan may show moderate uptake on blood pool images and mild uptake on static images. Hibernomas have increased uptake with $^{18}$F fluorodeoxyglucose positron emission tomography ($^{18}$F-FDG-PET) because of their high level of glucose metabolism rather than from tumor growth activity; therefore, $^{18}$F-FDG-PET can be useful to differentiate hibernomas from liposarcomas.

**Note:** Brown adipose tissue expresses glucose transporters and shows increased radiotracer uptake with $^{18}$F-FDG-PET, $^{99m}$Tc-methoxyisobutylisonitrile, $^{99m}$Tc-tetrofosmin, and $^{123}$I-meta-iodobenzylguanidine. $^{18}$F-FDG uptake within the neck and supraclavicular regions has previously been attributed to muscle activity because uptake was no longer demonstrated after the administration of muscle relaxants. Whereas radiotracer uptake in the supraclavicular region demonstrates a classic imaging appearance, uptake by brown adipose tissue within the chest and mediastinum may be mistaken for malignancies and lymphadenopathy.

**Pathology**

**Gross pathology:** Well circumscribed, encapsulated, soft, greasy to rubbery, and lobulated. The cut surface varies from yellow to red-brown depending on the amount of intracellular lipid and is occasionally mucoid with rare areas of hemorrhage. Maximum tumor dimension tends to be 5 to 10 cm; hibernomas reaching up to 20 cm in size have been reported.

**Microscopically:** Light microscopy typically shows the "hibernoma cells": large multivacuolated fat cells with finely vacuolated or granular cytoplasm, eccentric vesicular nuclei and a small single round central nucleolus having evenly dispersed chromatin. Abundant vascularity is characteristic and atypia is rare. Four histologic variants have been recognized based on the quality of hibernoma cells, the nature
of the stroma, and the presence of a spindle cell component.

Typical hibernoma (82%): Composed of a mixture of eosinophilic cells, hibernoma cells and pale cells (white fat cells) (figure 4).

Myxoid hibernoma (9%): Composed of multivacuolated cells with focal eosinophilic cytoplasm separated by a myxoid stroma. It occurs predominantly in males and the head and neck region. May be confused with myxoid liposarcoma; the hypervascularity, common presence of the prominent plexiform capillary pattern and characteristic t(12;16) molecular translocation help to diagnose myxoid liposarcoma from myxoid hibernomas.

Lipoma-like hibernoma (7%): Composed of scattered hibernoma cells among univacuolated mature adipocytes (figure 5).

Spindle cell hibernoma (2%): Composed of the typical multivacuolated cells observed in hibernoma, as well as adipocytes, spindle cells, mast cells, and collagen bundles. It is more common in the neck and scalp. CD34-positive spindle cells are present only in the spindle cell variant and also found in spindle cell lipoma.

Note: A hybrid tumor in the uterus of a 24-year-old woman having a smooth muscle component and a hibernomatous component has been reported and was termed leiomyohibernoma. An adenohibernoma comprised of brown fat and benign mammary glands has also been previously described.

Electron microscopy: Characteristic ultrastrutural features of brown fat are observed in the small vacuolated cells, including small, uniformly sized lipid droplets, numerous polymorphous mitochondria with dense inclusions, an external lamina that frequently is intact, and an intimate association with capillaries.

- Differential diagnosis

Lipoma, fibroma, rhabdomyoma, neurofibroma, angiolipoma, well-differentiated liposarcoma, giant cell tumor, metastatic carcinoma and hemangiomia; in children, one should consider rhabdomyosarcoma and lymphoma. Well-differentiated liposarcoma shows decreased vascularity and usually presents as a predominantly fatty mass having irregularly thickened,
linear, and/or nodular septa. Rhabdomyomas are distinguished by the complete absence of lipid vacuoles in the cytoplasm. Rhabdomyosarcoma is distinguished by its association with bone destruction, and lymphoma by the isoattenuated pattern in CT and isointensity to muscle on T1-weighted images.

**Treatment**

Complete surgical excision is the treatment of choice; in view of the benign tumor behavior, marginal complete excision is considered curative. Intralesional excision may be the only option for large tumors close to nerve or vessels; however, intralesional excision may result in continued growth and local recurrence.

Note: At surgery, the tumors usually are encapsulated and/or adherent to skeletal muscle of bone without invasion, and usually are encapsulated and easily separated from the surrounding soft tissues. No specific surgical considerations are required for surgical treatment of hibernomas further than standard oncological principles including careful dissection of adjacent nerves and vessels, and hemostasis. Hibernomas have the potential for significant bleeding during surgical excision. In this setting, embolization also becomes a consideration given the identification of large intratumoral vessels and the benign course of these lesions.

**Prognosis**

All hibernoma variants have the same good prognosis after complete excision. Metastases or malignant transformation have not been reported. Rare atypical mitoses, infiltrative pattern and intramuscular location are not necessarily criteria for malignancy.

**Cytogenetics**

**Cytogenetics Molecular**

The karyotypes of hibernomas are near-or pseudodiploid. There are structural rearrangements of 11q13-21 (most often 11q13), which are considered most characteristic, and a variety of partner chromosomes. This alteration can be detected by metaphase fluorescent in situ hybridization (FISH). However, 11q13 rearrangements also have been identified in other lipomatous tumors such as typical lipomas, infiltrative pattern and intramuscular location.

**Genes involved and proteins**

MEN1 gene (11q13.1) is most frequently deleted, while GARP gene (11q13.5) may also be involved. Loss of MEN1 and AIP tumor suppressor genes, that are located 3 Mb apart, and that underlie the hereditary syndromes pituitary adenoma predisposition and multiple endocrine neoplasia type I, is likely to be pathogenetically associated with hibernoma development.

**References**


This article should be referenced as such: Mavrogenis AF, Coll-Mesa L. Soft tissue: Hibernomas. Atlas Genet Cytogenet Oncol Haematol. 2013; 17(1):60-64.