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Research Article

# Observer Variation in the Diagnosis of Testicular Sex Cord-Stromal Tumors by a Genitourinary Pathology Society and International Society of Urological Pathology Panel: Paving the Way for a New Classification

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## ABSTRACT

The diagnosis of sex cord-stromal tumors is challenging. They show a wide spectrum of behaviors and associations with clinically important pathogenic germline variants. In view of recent advances in molecular subtyping and risk factors, we wished to investigate the differences in diagnosis for a range of these tumors using expert genitourinary pathologists with an interest in this area. Forty-four tumors were selected, and 18 pathologists (members of TEsticular Sex cord-Stromal Tumor group) were invited to view the cases online and give a diagnosis. Consensus was taken as 70% agreement. Consensus was achieved in 59% (26/44) cases. However, there were many areas of disagreement, which included variability in the diagnosis of Sertoli cell and Leydig cell tumors, particularly in malignant lesions, and difficulty in the assignation of fibrothecomas or myoid gonadal stromal tumors, as well as variability in the diagnosis of granulosa cell tumors and in the diagnosis of rarer pediatric tumors. Pathologists placed different weights on positivity with some markers, particularly beta-catenin, S100, and SMA. Some pathologists diagnosed novel diagnostic entities, such as inflammatory and nested testicular sex cord tumors, not currently in the World Health

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Organization classification. Recommendations to assist in the construction of a new classification to achieve more concordance and better treatment of these rare tumors are included.



## Introduction

Sex cord-stromal tumors (SCSTs) of the testis are rare and have extremely varied morphologic appearances.[1] From a clinical perspective, they range from entirely benign to aggressive and resistant to many lines of treatment, with the latter representing a relatively small subset (~10%).[2-4] Moreover, malignant potential seems to be restricted to specific histologic subtypes of testicular SCSTs as there are some that have never been reported to behave aggressively. Because predictors of clinical behavior remain incompletely understood, treatment decisions after excision can be challenging, and there are limited data to guide the need for (and extent of) postsurgical follow-up in individual patients. In this regard, it is currently unclear when adjuvant treatment, such as prophylactic retroperitoneal lymph node dissection, should be offered.[5] Another potential problem for clinical management is that some histologic subtypes of testicular SCSTs have been associated with inherited cancer predisposition syndromes; hence, the diagnosis of a SCSTs may indicate the need for genetic counseling and germline assessment in selected patients.[6-9] However, there are no formal recommendations to help clinicians decide which patients may need genetic evaluation.

From a diagnostic perspective, given their morphologic heterogeneity and rarity, testicular SCSTs are often challenging for pathologists to identify and classify. The classification of these tumors has been modified in the past decade, and there are differences in the schemes published by the World Health Organization (WHO)[10] and the Armed Forces Institute of Pathology (AFIP)[11] with continuing debate on the optimal methods and "rules" for proper categorization and treatment. Both classifications are based almost exclusively on morphology, with several tumor types being defined based on their morphologic resemblance to ovarian counterparts. However, given that the sex cord derivatives are different in the ovaries and the testes, and some homonymous ovarian and testicular entities exhibit significant clinical, molecular, and biologic differences, there is considerable room for further refinement of the current classification.

New molecular data have had a significant impact on our understanding of several SCST types. For instance, genomic analyses of Leydig cell tumors have demonstrated that they are molecularly heterogeneous, including a subset of cases associated with pathogenic fumarate hydratase variants.[8] Molecular data have also provided support for the existence of highly debated entities (such as Sertoli-Leydig cell tumor)[12] and identified seemingly novel testicular SCST types (such as malignant SCSTs with underlying *EWSR::ATF1*).[13]

For these reasons, both the International Society of Urological Pathologists and the Genitourinary Pathological Society cosponsored a consensus group of expert pathologists to work on this field of genitourinary pathology in order to achieve the specific goals mentioned below. The TEsticular Sex cord-Stromal Tumor group was formed in 2022, including experts in genitourinary pathology from North America, Europe, Oceania, and Asia. The primary goals of this group were to define by consensus, based on the best available evidence: (1) appropriate changes in classification, (2) recommendation for diagnostic workup of selected tumor types, and (3) recommendations for clinical management in selected scenarios for specific tumor types.

Because of the perceived differences in diagnosis of these tumors among expert pathologists, a major initial task of the group was to evaluate the haematoxalin and eosin slides of testicular SCSTs to determine the areas of concordance and discordance between the participants. This investigation of diagnostic divergence and areas of agreement would inform and enable improvement and refinement of future classifications with potential clinical impact on diagnosis and clinical management. Another objective of this exercise was to identify which of the currently defined entities can be reproducibly recognized based solely on the assessment of their morphology and which need supporting clinical, immunohistochemical, or molecular data for a definitive diagnosis. We expected that the results of the slide review would help us to evaluate the need for potential changes in classification, define supportive/desirable diagnostic findings, and recommend appropriate adjunctive tests for selected tumor types.

## Materials and Methods

Forty-four haematoxalin and eosin slides corresponding to 44 different testicular SCSTs were scanned onto an online server (based at Indiana University). The cases were gathered from the Robert Lane Tissue Bank Archives, at Queen Mary University of London and from the Indiana collections of Dr A.M. Acosta and Dr T.M. Ulbright. All slides were anonymized (Tissue Bank REC reference: 19/LO/0094). Slides were chosen to represent a range of entities and included straightforward and more challenging cases. Clinical history, patient age, and selected immunochemistry results were made available to all participants when appropriate. In specific cases, supporting immunohistochemical or clinical information was also purposely withheld to assess if these data were required to support the diagnosis.

Eighteen participants were invited for their previous interest and specialization in testicular stromal pathology and to represent a range of worldwide institutions.

Participants were asked to view the slides online and provide 1 preferred diagnosis per case. This was performed on the basis of free text rather than predefined fields, and users were able to add comments about potential differential diagnoses or weighted opinions. If it was not clear whether a single diagnosis was favored and the response was considered separately (ie, none of the entities included in the differential diagnosis were assumed to be favored at the time of computing the results).

Answers were collated, and consensus was achieved when more than 70% of participants agreed on a particular diagnosis (based on a pre-established threshold). All the slides are available for online review at: https://dsa.sca.iu.edu/dsa/#item/6557604447c4d992f4e5322f. Histories are provided in the results below. No immunochemical slides were provided, but

selected relevant results were given. Genetic results as well as knowledge of germline status (included in the description of the cases in Supplementary file S1) were not available to the participants.

The 70% consensus was taken because although 65% has been used as a consensus cutoff in previous the International Society of Urological Pathologist studies,[14] we thought a higher cutoff was more appropriate for this expert group.

## Results

Seventeen of the 18 of the experts provided answers. Although the majority of the cases had 17 responses, some cases received only 16 replies (Supplementary file S1) when fewer than 17 responses were received. Some consensus members failed to reach a definitive diagnosis on the case and gave a differential. These cases were not counted in the consensus even if they included the majority answer.

There was a consensus of 70% or over on 26/44 cases (59%). The details of the consensus of each separate case are provided in Supplementary Table S1. A list of the provided initial diagnoses and case histories (in the order they were presented to the panel) is shown in Supplementary Table S2, although it should be recognized, as mentioned, that many of these diagnoses predated the 2022 classification when a number of new entities were introduced and also the recent proposal for a number of other newer entities. A summary of the cases that achieved consensus is included in Table 1.

In summary, of the 12 Sertoli cell tumors, consensus was achieved in 8 (67%) with challenges on whether inflammatory nested sex cord tumor was a separate entity, on mixed forms, and on the use of the nuclear expression of beta-catenin as a diagnostic feature. Agreement was more difficult to achieve in the SCST not otherwise specified (NOS) or unclassified category where only 2/8 cases reached consensus (25%). However, consensus was also achieved in all 6 Leydig cell tumors. There were 5 cases of gonadal stromal tumor (GST). There was consensus on 3/5 cases if both fibrothecomas and myoid GSTs were combined, but only 1 case of a myoid GST achieved consensus on a specific subtype. Large cell calcifying Sertoli cell tumors achieved consensus in 50% of cases (2/4). The 3 juvenile granulosa cell tumors achieved 100% consensus.

No consensus was reached in 3 mixed SCSTs or Sertoli-stromal tumors. The single adult granulosa cell tumor achieved consensus; however, the entity was frequently diagnosed in many other cases by some experts.

No consensus was reached in the single cases of intratubular hyalinizing Sertoli cell tumor or Sertoli cell nodule. A comparison of the WHO fifth edition and AFIP fifth edition classifications (which show significant differences) has been included as well as an explanation of the potential changes and challenges associated with these diagnoses (Table 2).

Examples of 8 illustrative cases, reflecting the order of presentation in Table 1, and focusing on rarer and newer entities with the degrees of consensus are shown in Figures 1 to 8.

## Discussion

Both the WHO and AFIP have recently published updated classifications of testicular SCSTs, but neither incorporates new and important molecular findings. Over the last few years, the integration of molecular data and morphology has refined the classification of entities across different areas of pathology; the inclusion of molecular information may improve the classification and management of several histologic subtypes of SCSTs. Genomic analyses of testicular SCSTs have shown that some widely accepted tumor types can be well-defined based on molecular and morphologic features, whereas others are markedly heterogeneous and may not represent distinct entities.

Notwithstanding the recent molecular advances, morphology and immunochemistry alone can play a very important role in recognizing some tumor types, assessing the likelihood of tumor metastasis, and raising the possibility of underlying germline pathogenic variants. More specifically, some entities with recurrent genomic alterations may be easily recognizable by morphology (eg, Sertoli cell tumor), making molecular analyses unnecessary for diagnostic purposes. Nonetheless, adjunctive testing may be needed for prognostication or assessment of germline status. Hence, it is important to understand which of the established and new/emerging entities can be reproducibly identified based on their morphologic features and which require

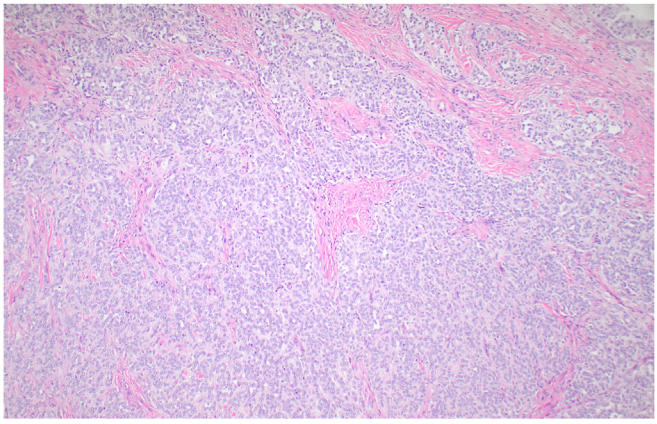

**Figure 1.**
(Case 29) This case achieved consensus on the diagnosis of a Sertoli cell tumor and on high-risk features. Although a consensus was possible in the majority of Sertoli cell tumors, Differences of opinion occurred on whether inflammatory nested sex cord tumor was a separate entity, mixed patterns, and use of immunochemistry for nuclear beta-catenin as a diagnostic feature.

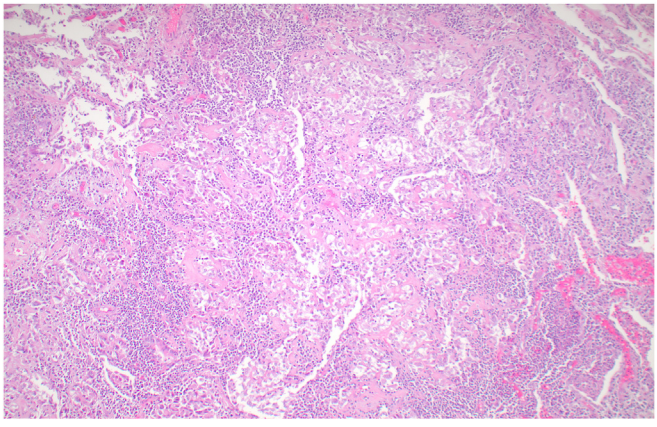

**Figure 2.**
(Case 18) This metastatic lesion to the lung failed to achieve consensus, although 8 of 17 (47%) diagnosed Inflammatory nested sex cord tumor. An ESWR fusion was proven in this case. This novel entity is not yet in the World Health Organization classification.

**Table 1**
Levels of consensus for each tumor type (not including malignancy risk)

| No. of cases | Type of tumor | Comment | Level of consensus reached and no. of case |
|---|---|---|---|
| 12 | Sertoli cell tumor (including inflammatory nested sex cord tumor) | Consensus was reached in 8/12 cases. Difficulties were on whether inflammatory nested sex cord tumor was a separate entity, mixed patterns including signet ring forms, and use of immunochemistry for nuclear beta-catenin as a diagnostic feature | 100%: case 30<br>90%-99%: cases 12 and 29<br>80%-89%: case 10<br>70%-79%: cases 11, 20, 27, and 37<br>No consensus: 3, 18, 31, and 32 |
| 8 | Sex cord-stromal NOS/ unclassified | Consensus was reached in 2/8 cases reflecting the challenging nature of this nonspecific category | 70%-79%: cases 2 and 21 (consensus for LCT).<br>No consensus 6 cases (6, 7, 13, 15, 26, and 40) |
| 6 | Leydig cell tumor | Consensus was reached in all cases | 90%-99%: cases 14, 41, and 42<br>80%-89%: case 43<br>70%-79%: cases 9 and 25 |
| 5 | Myoid gonadal stromal tumor/fibromathecoma | There was agreement on 3/5 cases if both subtypes were included into a single category; however, there was agreement on subtype on only 1 case (MGST) | 80%-99%: case 34<br>70%-79%: cases 1 and 33<br>No consensus: 5, 19 |
| 4 | Large cell calcifying Sertoli cell tumor | Consensus was reached in 2/4 cases | 100%: case 38<br>70%-79%: case 17<br>No consensus: cases 8 and 28 |
| 3 | Juvenile granulosa cell tumor | Consensus reached in all cases | 100%: cases 35 and 36<br>70%-79%: case 4 |
| 3 | Mixed sex cord-stromal tumor/ Sertoli-stromal tumor | No consensus was reached in these 3 cases, reflecting lack of definitions and controversy on use of these terms | No consensus: cases 22, 23, and 24 |
| 1 | Adult granulosa cell tumor | Consensus was reached in this case. However, adult granulosa cell tumor was also included as a differential or preferred diagnosis in other cases, highlighting that this entity may be overdiagnosed | 80%-89%: case 39 |
| 1 | Intratubular hyalinizing Sertoli cell tumor | No consensus reached, possibly reflecting rarity of the entity | No consensus: case 44 |
| 1 | Sertoli cell nodule | No consensus reached, possibly reflecting lack of criteria for diagnosis of the entity | No consensus: case 16 |

LCT, leydig cell tumor; MGST, myoid gonadal stromal tumor; NOS, not otherwise specified.

**Table 2**
Comparison of the WHO and AFIP classifications with the development and refinement issues for both

| Fifth edition WHO classification | fifth edition AFIP classification | Issues for development |
|---|---|---|
| Leydig cell tumor | Leydig cell tumor | Should a subset be reclassified as Fumarate hydratase-deficient SCST?<br>Should scoring system be introduced to assess malignancy? |
| Sertoli cell tumor | Sertoli cell tumors not otherwise specified.<br>- Sertoli cell Adenoma | Variation in methods of identifying Sertoli cell differentiation with use of pure morphology or use of immunochemistry.<br>Well-described malignant entity: “inflammatory nested sex cord tumor” is not in either classification |
| Large cell calcifying Sertoli cell tumor | Large cell calcifying Sertoli cell tumor | |
| Intratubular large cell hyalinizing Sertoli cell neoplasia | Intratubular large cell hyalinizing Sertoli cell neoplasia | |
| | Sertoli-stromal cell tumor | Encompassed by the “mixed sex cord stromal tumor” category in the WHO classification but is not molecularly distinct from other subtypes |
| | Sertoli-Leydig cell tumor | Encompassed by the “mixed sex cord stromal tumor” category in the WHO classification. Although the Leydig cell component may not be neoplastic in most cases, very rare tumors with *DICER1* alterations do include a neoplastic Leydig cell component |
| Adult granulosa cell tumor | Adult-type granulosa cell tumor | Lack of agreement in diagnosis on morphologic grounds in this survey. Should *FOXL2* mutation be the defining characteristic? |
| Juvenile granulosa cell tumor | Juvenile-type granulosa cell tumor | As these tumors are very different from their ovarian counterparts, a renaming emphasizing their benign nature is suggested |
| Tumors in the fibromathecoma group | Tumors in the fibromathecoma group | Experts could not reproducibly distinguish between myoid GSTs and fibrothecomas. Molecular differences between these tumors have not been identified. As they are both benign, and myoid GST is defined by coexpression of nonspecific markers, a category that encompasses both tumor types would be beneficial (eg, GST) |
| Mixed sex cord-stromal tumor | Mixed sex cord-stromal tumor | Overlap with Sertoli-stromal cell tumor and Sertoli-Leydig cell tumor (both included in the AFIP classification) |
| Sex cord-stromal tumor not otherwise specified | Unclassified sex cord-stromal tumor | See comment on fibrothecomas |
| Myoid GST | Myoid gonadal stromal tumor | See comment on fibrothecomas |

AFIP, Armed Forces Institute of Pathology; GST, gonadal stromal tumor; SCST, sex cord-stromal tumour; WHO, World Health Organisation.

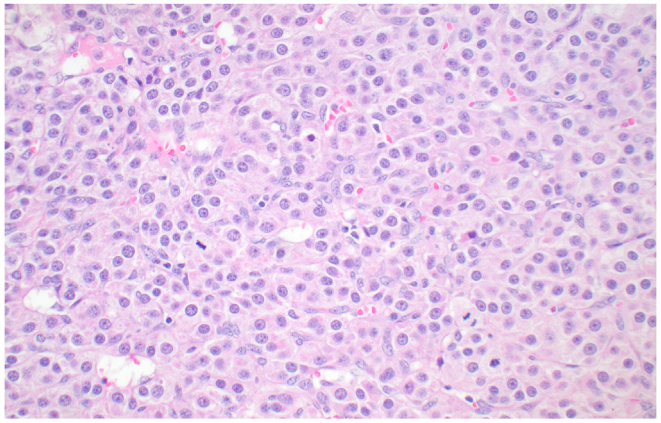

**Figure 3.**
(Case 31) There was no consensus on this malignant tumor originally diagnosed as a Sertoli cell tumor. Most (9/17, 53%) diagnosed malignant Leydig cell tumor, whereas 6 diagnosed Sertoli cell tumor, NOS and 2 sex cord-stromal tumor, NOS. NOS, not otherwise specified.

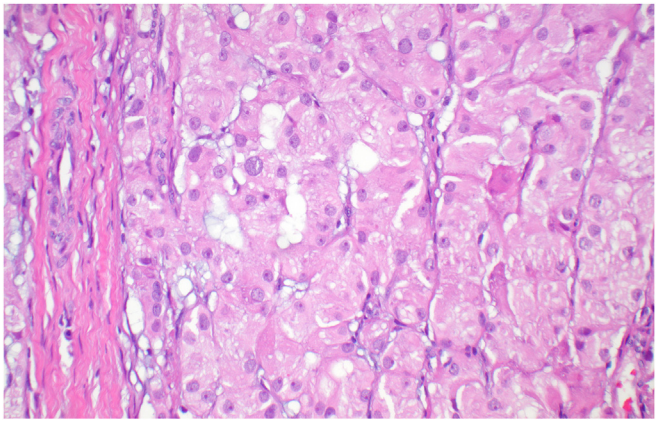

**Figure 5.**
(Case 28) This was a large cell calcifying Sertoli cell tumor in a known case of Carney's complex However, consensus was not reached in 50% of the large cell calcifying Sertoli cell tumors and in the single case of Intratubular Hyalinizing Sertoli cell tumor. The lack of calcifications may lead to challenges in diagnosis

further testing with immunohistochemistry or molecular studies. It is also crucial to assess whether potentially aggressive cases can be identified based on their appearances and immunoprofiles.

This consensus survey highlights areas where consensus is good and others where there is a need for clarity and guidance in diagnosis to facilitate good clinical management. We would emphasize that this collection of cases included very challenging scenarios, even for experts in the field, that some cases withheld important information (such as the history of inherited conditions), and also that we chose a high consensus of 70%. We would also emphasize that many consults come with limited workup and that many specialist immunochemical investigations (such as Steroidogenic factor 1) are not available in some laboratories and were not available on the older cases in this series. We would also emphasize that in 75% of cases, a majority (>50% participants) diagnosis was reached despite the challenges.

Among the areas of agreement, the most salient general conclusion is that typical Leydig and Sertoli cell tumors with indolent features (lacking significant atypia) can be reproducibly recognized by expert uropathologists. Similarly, large cell calcifying Sertoli cell tumors with typical histologic features can be reproducibly identified based solely on morphology. Also, there was significant agreement in identifying spindle cell tumors as "stromal tumors," but subclassification was less reproducible (see below).

Areas with disagreements that may need further consensus and clarity include the following.

1. Although tumors with a tubular or corded nature were usually classified as Sertoli cell tumors, there was divergence about the weight placed on diffuse nuclear beta-catenin staining to support this diagnosis. Although some experts were reliant on this immunochemistry, others were prepared to make the diagnosis more often in beta-catenin-negative tumors. Although patchy nuclear beta-catenin has been described in Leydig cell tumors,[15,16] diffuse strong expression appears to be somewhat specific for Sertoli cell tumor, NOS. Hence, more rigorous criteria for what type of beta-catenin staining is supportive of Sertoli cell tumor, NOS should be considered.
2. Although there was generally good consensus in the diagnosis of pure spindle cell tumors as GSTs, agreement on subtyping was only rarely achieved. Recent studies have failed to differentiate these tumors on molecular grounds,[12,17,18] and it has been pointed out that the 2 markers used for this, SMA and S100, lack sufficient specificity and sensitivity. Although most

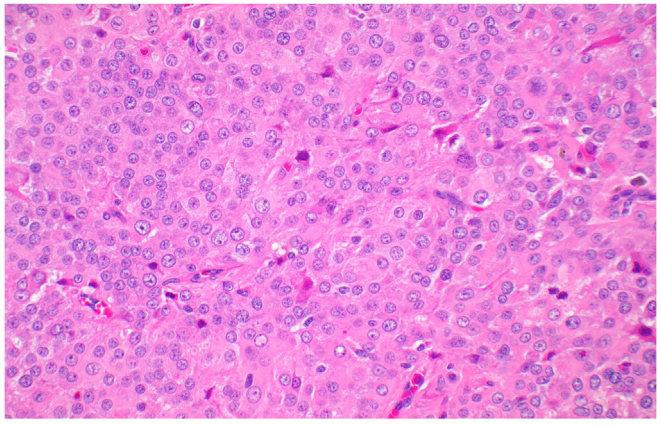

**Figure 4.**
(Case 42) There was consensus (16/17, 94%) that this represented a malignant Leydig cell tumor. There was an excellent consensus in Leydig cell diagnosis.

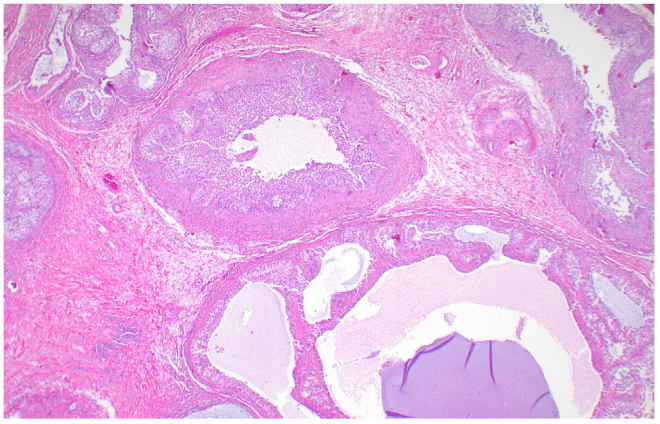

**Figure 6.**
(Case 35) There was 100% consensus that this was a juvenile granulosa cell tumor.

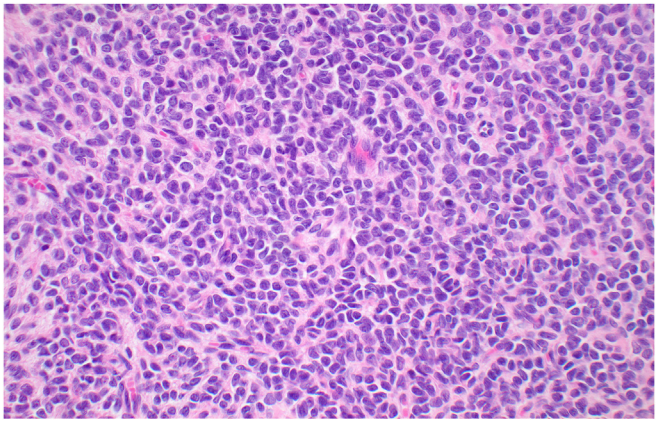

**Figure 7.**
(Case 39) There was consensus (14/17, 82%) for an adult granulosa cell tumor. This case harbored a *FOXL2* p.C134W variant demonstrated by DNA sequencing.

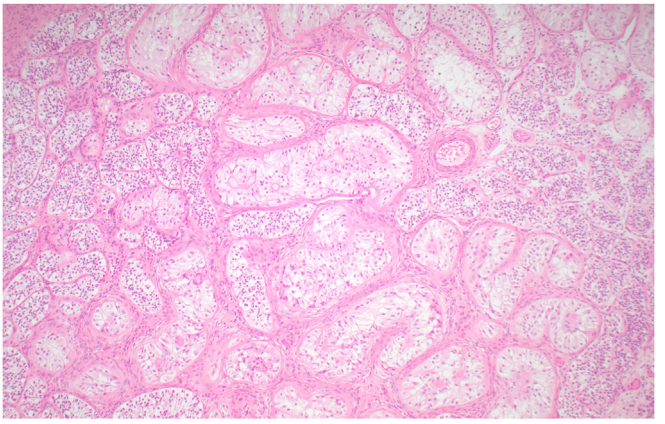

**Figure 8.**
(Case 44) There was no consensus, with most (10/17, 59%) diagnosing intratubular large cell hyalinizing Sertoli cell neoplasia (ILCHSCN). The remaining diagnoses included: 4 Sertoli cell nodules, 2 gonadoblastomas, and 1 Pick adenoma. This was a patient with Peutz-Jeghers syndrome and the lesion was an example of ILCHSCN with loss of STK11 expression identified by immunohistochemistry.

pathologists in the group support that myoid gonadal GST is a distinct entity, it seems difficult to distinguish between this tumor type and fibroma/thecoma. These results suggest that GST could be a useful umbrella term to use when a precise distinction between myoid GST and fibroma/thecoma is not possible. The grouping of both entities under a GST category is also reasonable from a clinical perspective because they are both indolent.

3. Among the tumors that were known to be malignant, although there was agreement on the presence of high-risk/aggressive features, there was frequently a lack of consensus over the tumor type. These differences were often the reason for a lack of consensus and guidance on what immunochemistry workup is appropriate for these neoplasms.
4. Sertoli-stromal cell tumors are included in the AFIP classification but not in the WHO classification. This caused a lack of consensus, depending on who was prepared to make this diagnosis in tumors with a mixed stromal and sex cord/Sertoli phenotype. Molecular data have shown that most of these tumors harbor genomic alterations similar to those seen in testicular SCST with pure or predominant spindle cell components, but there is a small subset with *CTNNB1* variants.[12]
5. Juvenile granulosa cell tumor was reproducibly diagnosed by most pathologists, with consensus in all cases. In contrast, variability was seen in the diagnosis of some important hereditary conditions (see point 7 below), with overdiagnosis of gonadoblastoma by some.
6. Except for 1 case with a hotspot *FOXL2* variant, there was little consensus for the diagnosis of adult granulosa cell tumor. A recent analysis has shown them to be molecularly heterogeneous, with only 1/13 cases showing the typical activating *FOXL2* pathogenic variant seen in the overwhelming majority of ovarian granulosa cell tumors.[19] This suggests that adult granulosa cell tumors of the testis are a contentious diagnosis and should probably be restricted to cases with prototypical morphology and/or supportive molecular results (if available).
7. Intratubular large cell hyalinizing Sertoli cell neoplasia was not easily identified without supportive clinical information. Similarly, large cell calcifying Sertoli cell tumors with unusual morphology (eg, absence of calcifications, fibrous rather than myxoid stroma, and subtle to absent neutrophilic infiltrates) were not consistently recognized. In addition, fumarate hydratase deficiency in Leydig cell tumors was not apparent based on the evaluation of morphologic features alone, and there was no consensus in several cases of inflammatory and nested testicular sex cord tumors. This suggests that clinical

**Table 3**
Consensus statements in SCSTs from the TESST group

1. The current classification of SCSTs (WHO 2022) is not aligned with the best available evidence because it excludes recently recognized entities that are clinically important, includes others that lack sufficient evidence to support their existence as distinct tumor types, and fails to define features that are desirable for diagnosing most tumor types
2. Standardization of terminology is required in the following areas:
   a. Gonadal stromal tumors
   b. Sertoli cell tumors
   c. Granulosa cell tumors
   d. Mixed SCSTs
   e. SCSTs associated with cancer predisposition syndromes
3. Several sex cord-stromal tumor types show high-frequency associations with specific genomic alterations, including some of germline origin. These should be acknowledged in an updated classification
4. Methods for assessing risk of malignant clinical behavior and the proper terminology used to address such risk need further standardization
5. Due to the complexity of this area and the importance of an accurate diagnosis for follow-up and treatment, we recommend referral to a specialist (genitourinary) pathologist when possible
6. The TESST group will work with ISUP and GUPS to provide evidence-based recommendations for diagnosis and management, as well as an updated classification of SCSTs in preparation for the sixth edition of the WHO blue book

GUPS, Genitourinary Pathology Society; ISUP, International Society of Uropathology; SCST, sex cord-stromal tumor; TESST, TEsticular Sex cord-Stromal Tumor group; WHO, World Health Organization.

information and molecular results are essential or important to support these diagnoses. Novel diagnostic immunochemical tests (such as PRKAR1A) and the wider availability of molecular analyses may aid with these diagnoses in centers with a high volume of testicular pathology.[20] Recommendations for diagnostic workups need to be suggested in the rarer but important area of pediatric SCST.

8. The language used to convey predicted clinical behavior based on the histopathologic findings showed significant variability among experts. Although this survey dealt primarily with tumor type, the terms “benign”/“low risk” or “malignant”/“high risk” were often used interchangeably, which may lead to clinical confusion. Recommendations about proper terminology should be issued in the future.
9. Finally, we would recommend that the difficulties and rarity of these tumors mean that they remain a challenge for experts. Therefore, general pathologists should have a low threshold for expert referral. This is mandated in some countries such as the United Kingdom, and as these tumors may only be encountered once or twice in a lifetime in general uropathological practice, a specialist referral is likely to highlight important inherited syndromes and the risk of metastasis.

A summary of the consensus statements arising from this survey is presented in Table 3.

The TEsticular Sex cord-Stromal Tumor group advocates a new classification for these tumors and will work together to produce a detailed consensus document outlining the methods by which these tumors should be diagnosed. This paper and the initial consensus statements form the basis and will guide a new classification.

We have shown that typical examples of Leydig cell tumor, Sertoli cell tumor, large cell calcifying Sertoli cell tumor, and juvenile granulosa cell tumor can be reliably identified based on morphology, justifying their existence as separate entities, with minimal workup needed for their classification. However, when these tumors exhibit unusual features, a workup to support the diagnosis is probably required (eg, a tumor without overt sex cord components and absence of nuclear beta-catenin expression is unlikely to represent a Sertoli cell tumor; a tumor without calcifications and/or neutrophilic infiltrates with retained PRKAR1A expression is unlikely to be large cell calcifying Sertoli cell tumor). There is a good agreement for recognizing GSTs, but not specific subtypes, suggesting that the inclusion of such a category/term (eg, gonadal stromal tumor, NOS) is probably justified and may avoid an unnecessary workup of these indolent tumors. Most *EWSR1:ATF1*-driven tumors were suspected based on their morphologic features, supporting that they represent a distinct entity and molecular testing should be done selectively. Finally, there is little to no agreement on the classification of adult granulosa cell tumor, which was frequently diagnosed by some in many examples of other tumor types, suggesting that this diagnosis should be restricted to lesions with prototypical morphologic features (as in the included case) and (ideally) supported by molecular results.

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*Author Contributions*

A.A. and D.M.B. led and initiated the survey wrote the paper and made revisions. M.C., E.C., K.C., A.G., S.G., J.C., M.I., C.-S.K., F.M., A.M., K.M., M.R.R., M.R.M., S.T., T.T., T.M.U., S.R.W., and P.G.-P. all participated in the survey. All authors gave intellectual input to the M.S., S.S. assisted in the data collection and analysis, and L.S. gave intellectual input and revisions regarding genetic basis of these tumors.

*Data Availability*

Details of the data analysis are available on reasonable request to DMB. All slides used in the study are freely available on line at the Indiana University Website (https://dsa.sca.iu.edu/dsa/#item/6557604447c4d992f4e5322f).

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*Declaration of Competing Interest*

The authors declare no competing interests pertaining to this paper.

*Ethics Approval and Consent to Participate*

All procedures were performed in compliance with relevant laws and institutional guidelines and have been approved by the appropriate institutional committee. This study was a consensus study using previous material only and no new work.

## Supplementary Material

The online version contains supplementary material available at https://doi.org/10.1016/j.modpat.2025.100804

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