

# A concise update on prostate pathology

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#### **SOUHRN**

Prostate carcinoma is the most common non-cutaneous malignancy in men in developed countries and the incidence has been steadily rising in the developing countries. Active research in recent years has led to tremendous progress in our understanding of the biology and genetics, and marked improvement in diagnosis and treatment of prostate cancer. Gleason grading has remained as the cornerstone for management of patients with prostate cancer. However, the grading system has continuously evolving since its inception in response to changes in the clinical practice of diagnosis and treatment of prostate cancer. The modification of Gleason grading system implemented by the International Society of Urological Pathology in 2005 has profoundly changed the way prostate cancer is graded and consequently how patients are managed. Several prostate cancer histological types with distinct clinical and pathological features have been rediscovered or redefined. Finally, elucidations of the molecular and genetic mechanism helps not only better understand the pathogenesis of prostate cancer, but also identify biomarkers for improved diagnosis, risk stratification and clinical management. This article briefly reviews the most recent advances in the Gleason grading system, new histological types and molecular genetics of prostate cancer.

Keywords: prostate - Gleason grade - intraductal carcinoma - neuroendocrine differentiation - molecular genetics

## Novinky v patologii prostaty

#### **SUMMARY**

Karcinom prostaty je (mimo kožních nádorů) nejčastější malignitou mužů v rozvinutých zemích a jeho incidence v rozvojových zemích stále roste. Aktivní výzkum v posledních letech výrazně napomohl porozumění biologie a genetiky karcinomu prostaty, vedl ke zlepšení jeho diagnostiky i léčby. Gleasonův grading stále hraje v nastavení léčebné strategie pacientů s karcinomem prostaty zásadní roli. Tento grading se však od začátku vyvíjí a odráží tak postupné změny v klinické praxi. Modifikovaný Gleasonův grading byl zaveden v roce 2005 a výrazně změnil způsob, jakým je grade karcinomu prostaty stanovován, i způsob, jakým je pacient poté léčen. Několik histologických typů karcinomu prostaty s odlišnými klinickými a patologickými znaky bylo nově objeveno nebo předefinováno. Konečně, pochopení molekulárních a genetických mechanismů pomáhá nejen lépe porozumět patogenezi karcinomu prostaty, ale také identifikovat biomarkery pro lepší diagnostiku, stratifikaci rizika a klinický management onemocnění. Tento text stručně shrnuje nejnovější změny v Gleasonově gradingu, nové histologické typy a molekulární genetiku karcinomu prostaty.

Klíčová slova: prostata - Gleasonovo skóre - intraduktální karcinom - neuroendokrinní diferenciace - molekulární genetika

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Prostate carcinoma (PCa) is the most common non-cutaneous malignancy in men in developed countries and the incidence has been steadily rising in the developing countries as well (1). Active research has led to tremendous progress in our understanding of the biology and genetics, and marked improvement in diagnosis and treatment of PCa in the last decade. This article briefly reviews the most recent advances in the Gleason grading system, several PCa histological types that have been recently redefined and molecular genetics of PCa that are most relevant to surgical pathologists' practice.

### **CONTEMPORARY GLEASON GRADING SYSTEM**

Gleason grading system, developed by Dr. Donald Gleason in 1967 (2,3), remains as the cornerstone for the management of

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Ming Zhou, MD, PhD NYU Langone Medical Center Tisch Hospital 560 First Avenue, TCH-461 New York, NY 10016-6497, USA phone: 646-501-6976 fax: 212-263-7916 email: ming.zhou@nyumc.org prostate cancer. The system is relatively simple and reasonably reproducible to apply (4,5). It is one of the key parameters for planning treatment, and remains as the most important prognostic factor in predicting pathological findings in radical prostatectomy (RP), biochemical failure, local and distant metastasis after therapy and PCa specific mortality.

The Gleason grading system has undergone continuous modification and changes in response to changes in the clinical practice of diagnosis and treatment of prostate cancer since its inception (6). The most significant changes were introduced in 2005 at the auspices of the International Society of Urological Pathology (ISUP) (7) and further modification also ensued (Fig. 1) (4). The resulting contemporary grading system is referred to as "2005 ISUP modified Gleason grading system". However, it is important to stress that the changes put forth by ISUP simply codified what have already been used in practice by many pathologists. It is important for surgical pathologists to be acquainted with and apply the modified grading criteria in their practice.

# Important changes in 2005 modified Gleason grading system

Some of the changes are definitional, including precise definition of each Gleason grade and grading criteria for PCa morphological variants. Others are operational, i.e., how to report Gleason grade in special circumstances, including reporting of secondary