（第6版）

临床肿瘤学手册

MANUAL OF CLINICAL ONCOLOGY

主编 〔美〕Dennis A. Casciato

主译 刘云鹏 李 智

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Manual of Clinical Oncology

(Sixth Edition)

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译者的话

近20年来，全世界范围内恶性肿瘤的治疗取得了显著进步，肿瘤病死率的降幅达到15%，有2/3的患者的生存期长于5年。分析其原因，一方面，化疗药物和化疗方案及放疗技术都取得了显著进步。另一方面，特别是近10年来，以EGFR、VEGF及Her-2等分子为靶点的分子靶向治疗使疗效进一步提高。恶性肿瘤的治疗进入到规范化与个体化并行的时代。我国恶性肿瘤的治疗同期也取得了长足的进步。但是，随着人口老龄化以及生活方式、环境的改变，恶性肿瘤仍然是威胁人类健康的主要“杀手”。据卫生部《2009中国卫生统计年鉴》报告，1990年至2008年间，在城市和农村，恶性肿瘤占人口死因的比例分别由18.16%和13.96%增至23.49%和20.06%，位次分别由原来的第二、第三位上升至第一和第二位。恶性肿瘤的防治形势依然严峻。

作为临床医生，我们常常处在相互矛盾的现实中。一方面，随着科学进步不断出现新的药物与方法，为我们带来令人欣喜的更多的选择；但另一方面，科学进步也使我们对疾病的异质性的认识越来越深刻，多种方法并存也增加了治疗决策的难度。如何选择适合的患者，在恰当的时机，给予合适的药物，如何更好地控制疾病本身和治疗相关的并发症，如何更好地平衡疗效与高涨的医疗费用之间的关系，如何进行充分的医患沟通等等，对医生的要求越来越高。为了使相关领域的同道在浩瀚的文献海洋中，快速准确地借鉴最有价值的研究结果，为治疗决策提供有价值的参考，我们应出版社邀请，翻译了这本《临床肿瘤学手册》。

本书自上个世纪第1版面世以来，迄今已是第6次改版。正如本书的主编Dennis A. Casciato在前言中所述，本书是“备受肿瘤界同仁、住院医师和医学生关注与好评的临床参考书”。本书的特点是简洁、清晰和实用，在放射肿瘤学方面，尤具特色。我们相信，本书也能为我国的肿瘤相关专业的医务人员、研究生和科研人员提供参考。

在翻译过程中，我们遵循力争保留“原汁原味”的原则，书中的数据以及药物剂量、用法等等完全忠实于原文，以突出原著的特点，但未必适于东方人种和我国国情，望读者审慎地借鉴应用。本书的译者由工作在临床一线的教授和中青年医生组成。另外，还有多名科研人员在翻译和审校过程中付出了很多辛苦，她们是：澳大利亚西澳大学李林博士、中国医科大学附属一院肿瘤内科医生罗颖、张凌云和输血科周文玲以及肿瘤学研究生王瑾、潘虹、卜欣，在此一并表示衷心感谢。由于东西方的语言习惯差异以及专属名词的特殊性，译书中难免存在错误和不妥之处，欢迎各界同仁批评、指正。

刘云鹏　李　智

第6版前言

《临床肿瘤手册》是一本备受肿瘤界同仁、住院医师和医学生关注与好评的临床参考书，此次第6次改版，对内容进行了全面修订。遵循与前期版本相同的风格，本版仍强调实用性，即对肿瘤患者的床边诊断与治疗决策的制定提供有用的信息。本手册致力于将最广、最新且经得住时间考验的诊疗信息用简明扼要的语言呈现于广大读者面前，在避免赘述的同时摒除诸如化疗的“每月方案”之类过时的肿瘤学术语。

本书共分四部分，第一部分主要介绍肿瘤诊断和治疗的总体原则。第二和第三部分采用统一的文章结构详细介绍各系统恶性肿瘤。第四部分以受累终末器官为单元详述肿瘤并发症，包括局部浸润、转移、副肿瘤综合征及治疗相关的并发症。附录介绍了细胞遗传学术语（附录A）；化疗并发症以及临床试验的毒性评价标准（附录B）；肿瘤评价指标，如用于鉴别诊断的免疫组化指标、白细胞分化抗原、世界卫生组织关于造血系统恶性肿瘤的分类原则等（附录C）；以及淋巴瘤的最常用化疗方案（附录D）。

本书第1版几乎全部由Barry Lowitz博士和本人完成。后续版本中新作者的加入扩大了本书编著人员的专业及地域分布。另外，主编细致入微的审校，确保了本书在结构、内容、风格和逻辑上的一致性。在此，谨对Bartosz Chmielowski博士、Nancy Klipfel博士、Dan Leibovici博士、Theodore Moore博士、Ron Paquette博士、Mark Pegram博士、Lauren Pinter－Brown博士、Antoni Ribas博士、Gary Schiller博士、Eric Sherman博士及Przemyslaw Twardowski博士等作为“首次”为本版书的编纂完成所做的重要贡献表示衷心的感谢。同时非常荣幸能邀请到我的朋友及同事Mary Territo博士作为本书的副主编。感谢她为造血系统恶性肿瘤的改编所做出的巨大贡献。

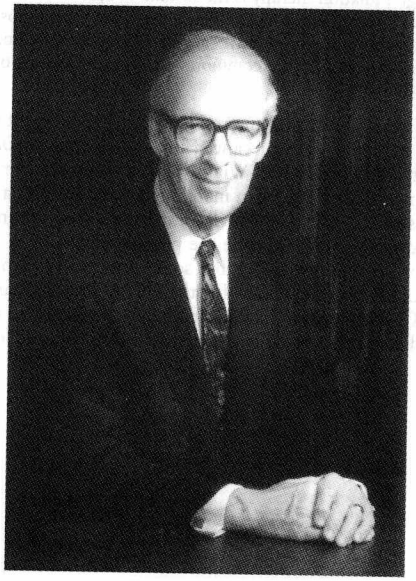
肿瘤治疗涉及临床、心理及社会多种诊疗模式的参与，单纯基于任一方面的有限资料所做出的治疗决策均是片面的。每个患者都有其独特性，其疾病发展过程几乎没有约定俗成的范例可循。肿瘤的复杂性和不可预知性使其治疗决策成为一件高雅的艺术作品，体现了科学知识、个人经验、常识以及系统评价结果的精炼与平衡。

第6版《临床肿瘤学手册》重申了医患关系的独特性，继续致力于培养提高健康管理者的综合诊疗护理水平，提倡通过结合当今先进的诊疗技术、合理的病情判断以及严谨开放的态度为癌症治疗带来曙光。

Dennis A. Casciato

（李　智译　刘云鹏审校）

Robert G. Parker, MD
January 29, 1925–March 31, 2005



Dr. Parker was a pioneer in the field of Radiation Oncology. In fact, he was one of the founding fathers of the discipline that seceded from its cousin, Diagnostic Radiology.

Dr. Parker received his college education at the University of Michigan and earned his Doctor of Medicine degree from the University of Wisconsin in 1948. After internship at the University of Nebraska, he fulfilled residency training in pathology at Western Reserve University and then completed a residency in radiology at the University of Michigan. He subsequently completed postdoctoral work at the Tumor Institute of the Swedish Hospital in Seattle, Washington, and pursued further postgraduate education in nuclear medicine at Columbia University.

From 1958 to 1977, he served as the Director of Therapeutic Radiology at the University of Washington. He was the founding chairman of the Department of Radiation Oncology at the University of California at Los Angeles in 1977, and he served in that capacity until 1994. He remained active clinically until his retirement in January, 2005.

Dr. Parker achieved a long list of academic accomplishments, including publication of more than 155 peer-reviewed articles and 43 book chapters. He was the lead author for Chapters 3 and 7 for this *Manual of Clinical Oncology* since its second edition. He also held visiting professorships at many major universities in the United States and abroad and was invited to deliver numerous prestigious lectureships.

He served as the President of several leading professional organizations, including the American Society of Radiology and Oncology (ASTRO), the Radiological Society of North

America (RSNA), the American Board of Radiology (ABR), and the American Radium Society (ARS), all of which have honored him with either a gold medal or life-achievement recognition.

A true gentleman and scholar, Dr. Parker represents the aggregate epitome of a clinical scientist, an effective educator, and a compassionate physician. His legacy in the field of radiation oncology is perhaps best portrayed by his presidential address for ASTRO in 1976:

> Each of you has made a primary responsibility to humans afflicted by cancer. Such a responsibility requires interests far beyond what is included in a restrictive definition of therapeutic radiology. Indeed, your highest responsibility is to reduce the frequency of or even eliminate cancer, even though radiation therapy is the sustaining base of your current intellectual and economic activities. Thus maintenance of your recognized central position in clinical cancer activities ultimately will not rest on advocacy of a treatment method, but on a myriad of activities which have an underlying common objective of reducing or even eliminating the need for such treatment.

As witnessed by medical students and residents, Dr. Parker spent most of his time with patients in the clinic talking not about cancer, but rather about *living*. In private life, he once scrimmaged with the Detroit Red Wings, played trombone for the Woody Herman Orchestra, led the University of Michigan marching band, and was a gourmet cook and a jazz piano player. His office at UCLA was decorated with magnificent photographs taken from his trips around the world. He made the physicians at UCLA use blue and gold as background colors for presentation slides, but some continue to suspect that it was meant for the Michigan Wolverines rather than for the UCLA Bruins. During the memorial to celebrate his life at UCLA on June 23, 2005, friends and distinguished scholars from all over the country came and paid tribute to this wonderful human being so loved by everyone. We miss you, Professor!

Steve P. Lee, MD
For the Editors

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The Editor extends his most sincere gratitude to Eve Perkins and her staff for their continued assistance to the *Manual of Clinical Oncology*. Eve is the medical librarian at Northridge Hospital Medical Center in Northridge, California. Her literature searches for me were indispensable. I also graciously thank Anne E. Jacobs, Senior Managing Editor for Medicine at Lippincott Williams & Wilkins, and Donna Kessler of Aptara, Inc. for their personal support and efforts to make this publication a success.

Dennis A. Casciato, MD

It is not hard to compose,
but it is wonderfully hard to let the superfluous notes
fall under the table.

—Johannes Brahms

No passion in the world is equal to the passion to
alter someone else's draft.

—H.G. Wells

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目录

第一章 概 要

第一节 原则、概念和统计学

Barry B. Lowitz Dennis A. Casciato

一、肿瘤生物学与肿瘤治疗原则

（一）正常细胞增殖

1. 细胞增殖 细胞的复制要经历几个时相（图1），这些时相由外界刺激引发、受到内部和外部生长因素调控。这个过程中同时存在特定癌基因和细胞周期特异性蛋白的激活和失活。放疗或者化疗主要对进入细胞周期的细胞具有杀伤作用。许多细胞毒性药物作用于细胞周期的多个时相，包括被分类为细胞周期特异性的药物。

（1）G_0 期（gap 0 或休止期），细胞通常按程序执行其特定功能，特异性作用于此期的药物如对成熟淋巴细胞起作用的糖皮质激素。

（2）G_1 期（gap 1 或分裂间期），细胞合成执行其特异性功能的蛋白质和 RNA。在 G_1 晚期，RNA 大量合成，并产生许多 DNA 合成所必需的酶。此期的代表性药物是左旋门冬酰胺酶。

（3）S 期（DNA 合成期），细胞内 DNA 倍增。此期的代表性药物是抗代谢药和甲基苄肼。

（4）G_2 期（gap 2），DNA 合成停止，蛋白质和 RNA 继续合成。有丝分裂纺锤体的微管前体已经开始形成。此期的代表性药物是博来霉素和植物碱类。

（5）M 期（有丝分裂期），遗传物质进入子代细胞后，蛋白质和 RNA 合成的速度明显下降。在完成有丝分裂后，新的细胞进入 G_0 期或 G_1 期。作用于此期的代表药物是植物碱类。

2. 细胞周期素 可以激活细胞周期的各个时相。大部分有复制能力的正常细胞可对外界刺激发生反应而增殖。比如生长因子、某些激素、组织相容性抗原复合体均可作用于细胞表面受体，通过细胞内信号传导诱导细胞分裂。从细胞外生长因子到细胞核的细胞增殖信号级联中，酪氨酸激酶是不可或缺的一部分。细胞周期素可以结合、激活并调节特异性酪氨酸激酶的功能，这些酶被称为细胞周期素依赖性激酶。

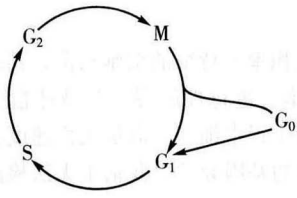

图 1.1 细胞周期

3. 细胞周期检测点　具有自我复制能力的细胞通常可停在细胞周期中的特定时期，这些特定时期叫做检测点。其中，最重要的是 DNA 合成起始点以及有丝分裂前检测点。这些组织学静止期可能与细胞周期素相关激酶的活性减低以及肿瘤抑制蛋白的调节相关。实际上，此时细胞仍然有生化学活性，在为进入下一时期生产蛋白质，并在自我复制前修复基因缺陷。

（1）正常细胞具有检测 DNA 序列异常的机制。当发生 DNA 损伤时，一系列修复机制可利用正常分子取代受损核苷酸。这些机制对于细胞的自我复制至关重要，可确保子细胞中的遗传物质与母细胞完全相同。

（2）第一个检测点位于 G_1 期末，S（合成）期前。即使接收到适宜的细胞外信号，而且 DNA 的合成准备就绪，DNA 还必须处于无损伤的可复制状态，细胞方可结束 G_1 期进入下一期。检测到 DNA 损伤时，细胞或者进行损伤修复，或者发生凋亡。该检测点是 p53 蛋白的作用点之一。

（3）第二个检测点位于有丝分裂期（M）前，细胞周期抑制因子将细胞停在此处，直到确认新的子代从母代精确无误地获得遗传信息。DNA 未能完全、精确复制，或者蛋白质、纺锤体等准备不足时，细胞将停在该检测点，直到万事俱备，细胞方进入有丝分裂期。

4. 正常的细胞群中有一小部分叫做“永生细胞”，可被机体其他部位的信号激活，发生自身复制，并可产生成熟的子细胞，后者可分化为特异性组织细胞，以满足整个机体的功能需要。尽管某些组织细胞可发生去分化，但是多数细胞分化后即失去永生能力，进入衰老阶段，最终死亡。真核细胞中可鉴定出如下四种正常的永生细胞。

（1）生殖细胞　能够无限的自我复制，可能与其进行减数分裂相关。与肿瘤细胞不同，此类细胞必须通过减数分裂方能产生永生细胞系。

（2）干细胞　这种细胞仅有两个功能，一是自我复制，二是产生分化成熟并执行宿主特殊功能的细胞。与肿瘤细胞不同，此类细胞的增殖周期有限。

（3）部分分化细胞　自我复制能力有限，最终产生分化完全、无再生能力的子代细胞。

（4）完全成熟的特异性细胞　不能复制产生子代。

5.“分化”是与“永生”完全相反的细胞状态。与肿瘤细胞系的永生定义不同，分化正常的细胞具有生物钟，可计算细胞分裂次数，到达一定次数后细胞不再进行分裂。例如，培养的人类成纤维细胞可以分裂大约 50 次，此后，无论提供何种养分及环境，均不再有细胞分裂发生。

（二）肿瘤细胞的特征

肿瘤可被定义为以进行性的细胞团块积聚为特征的细胞紊乱，其结果是细胞的过度增殖超过正常的细胞丢失；这些细胞会进行性的侵入和破坏宿主的组织和器官。肿瘤细胞虽属异常细胞，死亡速率快于正常细胞，但是死亡速度仍较细胞新生的速度慢。这种不平衡缘于肿瘤细胞本身的基因异常以及宿主无法检测和破坏肿瘤细胞。肿瘤细胞的独特性如下：

1. 克隆起源　多数肿瘤细胞起源于单个异常细胞。某些肿瘤起源于多个恶性