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Дозиомика в анализе медицинских изображений и перспективы её использования в клинической практике

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АННОТАЦИЯ

Обоснование. В последние годы увеличивается количество статей с использованием термина «дозеомика», однако литературные обзоры на русском языке по данной теме отсутствуют.

Цель настоящего обзора — описать основные принципы дозеомики как направления радиомики и проанализировать исследования по оценке возможностей применения их в клинической практике.

Материалы и методы. Систематический поиск литературы был произведён в базе данных PubMed с поисковым запросом «dosiomics OR dosiomic», а также в базе данных eLibrary с поисковым запросом «дозеомика». По состоянию на апрель 2023 года были опубликованы 43 зарубежных исследования на тему использования дозеомики в клинической практике и одна отечественная работа с определением термина «дозеомика».

Результаты. Проанализированы 43 зарубежных исследования на тему использования дозеомики в клинической практике и 1 отечественная статья с определением термина «дозеомика». Проанализированные работы разделены на три группы согласно их тематике и составлены таблицы, описывающие результаты 27 исследований по прогнозированию клинических исходов.

Заключение. В настоящее время дозеомика является новым и перспективным направлением радиомики, применяемым в текстурном анализе медицинских изображений, связанных с лучевым лечением онкологических больных. Дозеомика может способствовать развитию более персонализированного подхода к планированию лучевой терапии, прогнозированию лучевых повреждений нормальных тканей и диагностике рецидивов.

Ключевые слова: дозеомика; радиомика; лучевая терапия; машинное обучение; искусственный интеллект; текстурный анализ; постлучевой пневмонит.

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Dosimomics in the analysis of medical images and prospects for its use in clinical practice

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ABSTRACT

BACKGROUND: In recent years, there has been a notable increase in the number of articles using the term “dosimomics”. However, there are no literature reviews on this topic in the Russian language.

AIM: This study aims to describe the basic principles of dosimomics as a derivative of radiomics and to analyze studies devoted to assessing the possibilities of its application in clinical practice.

MATERIALS AND METHODS: A systematic literature search was performed in the PubMed database using the search query “dosimomics OR dosiomic”, and in the eLibrary database using the search query “dosimomics”. By April 2023, 43 foreign articles and 1 Russian article had been published.

RESULTS: The analysis encompassed 43 foreign studies investigating the use of dosimomics in clinical practice, alongside one Russian article that provided a definition of the term “dosimomics”. The analyzed papers were divided into three groups according to their subject matter, and two tables describing the results of 27 studies on the prediction of clinical outcomes were created.

CONCLUSION: Currently, dosimomics is a new and promising derivative of radiomics used in the textural analysis of medical images associated with radiation treatment of cancer patients. Dosimomics can contribute to the development of a more personalized approach to the planning of radiotherapy, the prediction of radiation damage of normal tissues, and the diagnosis of recurrence.

Keywords: dosimomics; radiomics; radiation therapy; machine learning; artificial intelligence; texture analysis; radiation pneumonitis.

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医学图像分析中的剂量组学及其在临床实践中的应用前景

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简评

论证。近年来，使用“剂量组学”一词的文章数量不断增加，但却没有关于这一主题的俄文文献综述。

本综述的目的是描述剂量组学作为放射组学分支的基本原理，并分析相关研究，以评估其在临床实践中的潜在应用。

材料和方法。在PubMed数据库中以“dosimics OR dosimic”为检索词进行了系统文献检索，在eLibrary数据库中以“дозимика”（剂量组学）为检索词进行了系统文献检索。截至2023年4月，共发表了43项关于在临床实践中使用剂量组学的国外研究和1篇定义“剂量组学”一词的国内文章。

结果。我们分析了43项关于在临床实践中使用剂量组学的国外研究和1篇定义“剂量组学”一词的国内文章。我们将所分析的文章按主题分为三组，并将27项关于预测临床结果的研究结果编制成表格。

结论。目前，剂量组学是放射组学的一个新的有前途的分支，应用于与癌症患者放射治疗有关的医学图像的纹理分析。剂量组学可能有助于开发更个性化的放疗计划、预测对正常组织的辐射损伤和诊断复发。

关键词：剂量组学；放射组学；放射治疗；机器学习；人工智能；纹理分析；放疗后肺炎。

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绪论

放射治疗是癌症患者最广泛使用的治疗方法之一。放射治疗可作为一种独立的治疗方法，也可以将其与手术或化疗结合使用，但放射治疗后出现并发症的风险较高[1]。因此，毒性评估是放射治疗计划和实施的一个重要方面[2]。

应对这一挑战的方法之一是为每位患者量身定制剂量（例如，为低风险的患者增加剂量，或为并发症高风险的患者优化治疗[2]）。具体办法是在放疗计划阶段就构建预后模型，以在各种指数的基础上对健康器官和组织遭受辐射损伤的风险进行评估。

目前放射组学（Radiomics）被广泛应用于放射学检查数据分析领域：放射组学是一种基于机器学习从医学图像中提取定量特征（通常是形状、强度和纹理描述）的方法，医学图像数据可用于构建预后模型[3]。

放射组学被广泛用于诊断不同类型的胸部器官疾病：结节性肿块和癌症、阻塞性和限制性疾病、浸润性肺部疾病等领域[4-7]。此外，放射组学还被成功用于预测治疗副作用（如放疗和免疫疗法引起的肺炎）以及区分医源性肺损伤和肿瘤复发[7]。放射组学已被广泛用于预测 COVID-19 的病程[8-10]。放射组学的应用会提高诊断、预后、治疗、随访和治疗反应监测的效率[11]。

除了放射组学以外，“剂量组学”（Dosiomics）的概念也越来越多地被使用：剂量组学是放射组学的一个分支，应用于放射治疗的三维剂量分布，以提取有用的特征来预测放射治疗的结果[12-14]。如今，根据剂量组学、放射组学和患者临床数据预测放疗后损伤发展的综合方法越来越受欢迎[13]。

本综述的目的是描述剂量组学作为放射组学分支的基本原理，并分析相关研究，以评估其在临床实践中的潜在应用。

搜索条件和纳入标准

在PubMed数据库中以“dosiomics OR dosiomic”为检索词进行了系统文献检索，在eLibrary数据库中以“дозимика”（剂量组学）为检索词进行了

系统文献检索。截至2023年4月，共发表了43项国外研究和1项国内研究。

因此，我们分析了43项关于在临床实践中使用剂量组学的国外研究和1篇定义“剂量组学”一词的国内文章[15]。我们将所分析的文章按主题分为三组，并将27项关于预测临床结果的研究结果编制成表格。

放射组学和剂量组学的基础：从计算机断层扫描图像中提取纹理特征的方法

通过多变量统计分析，放射组学允许确定器官和组织医学影像的众多定量特征与疾病临床表现之间的关系[16]。

放射组学指数描述组织图像的纹理特征，可用于识别图像生物标志物和构建预测性经验法则[17]。

图1给出以肺部计算机断层扫描（CT）为例，提取和分析放射组学参数的步骤。放射学检查后，对感兴趣区域进行分割。这一操作可将病变从周围的健康组织中分离出来。三维（3D）分割可以提供更多信息，特别是对于空间异质性和高体积的病灶。分割方法包括手动、半自动和全自动方法[16, 18]。接下来，通过数学算法计算目测评估无法获得的放射组学指数。指数通常包括一阶统计量、半色调邻接矩阵和均匀矩阵。最后一步是降低样本维度、进行统计分析和选择最重要的特征，并排除相关值。在此基础上，使用机器学习方法构建决定性规则[18]。

放射组学的主要指数

放射组学指数是利用公开PyRadiomics库从医学图像中提取的。放射组学包括两大类指数：一阶统计量（First-order statistics）和基于纹理邻接矩阵和均匀矩阵。这些矩阵包括[16-18]：

- GLCM (Gray Level Co-occurrence Matrix) —— 灰度共生矩阵；
- GLRLM (Gray Level Run Length Matrix) —— 灰度游程矩阵；

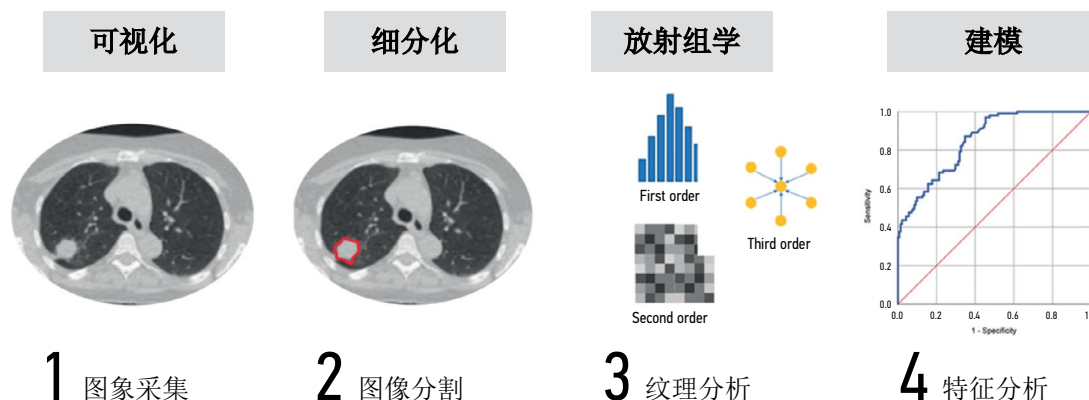


图1. 提取和分析放射组学指数的步骤。

- GLSZM (Gray Level Size Zone Matrix) —— 灰度区域大小矩阵;
- NGTDM (Neighbouring Gray Tone Difference Matrix) —— 邻域灰度差矩阵;
- GLDM (Gray Level Dependence Matrix) —— 灰度相关矩阵。

一阶统计量描述给定兴趣区域内像素强度直方图上灰度的频率分布, 而不考虑像素之间的空间关系[19]。由于这些特征基于对单个像素或单个体素的分析, 而不考虑周围区域的强度, 因此被称为一阶统计量。

下列阶次的统计量考虑到空间中体素的相互排列。它们能够描述纹理特征。其中最常见的是半色调邻接矩阵和均匀矩阵: GLCM、GLRLM、GLSZM。NGTDM和GLDM矩阵则不太常见。

灰度共生矩阵 (GLCM) 是灰度的二阶直方图[19]。它捕捉像素对或体素对的空间关系, 这些像素对或体素对在不同方向 (二维分析时为水平、垂直或对角线方向, 三维分析时为13个方向) 具有预定义的灰度强度, 像素或体素之间具有预定义的距离 (图2; 下文将介绍在二维空间计算矩阵指数的原理) [20]。

GLRLM为灰度游程矩阵, 由M.M.Galloway描述, 它提供在二维或三维中一个或多个方向上具有相同灰度的连续像素向量的空间分布信息 (图3) [19-22]。

GLSZM为灰度区域大小矩阵, 定量描述图像中由相邻体素组成的具有相同灰度的区域。根据G.Thibault等人[23], GLSZM的原理类似于GLRLM。但GLSZM基于对具有相同灰度的相邻像素或体素相互连接的组群 (所谓区域) 数量的计数 (图4)。纹理越均匀, 矩阵就越宽和平坦。GLSZM不针对不同方向进行计算, 但可针对确定领域的像素或体素之间的不同距离进行计算。GLSZM特征可在二维 (8个相邻像素) 或三维 (26个相邻体素) 中计算[19]。

NGTDM为邻域灰度差矩阵。该矩阵的纹理特征反映相邻体素之间的强度差异[24]。

灰度相关矩阵 (GLDM) 定量描述图像中的灰度相关关系[19, 25]。

剂量组学

剂量组学剂量组学是放射组学领域的一个新分支。剂量组学是对用于计划放射治疗的辐射剂量分布计划进行的纹理分析。

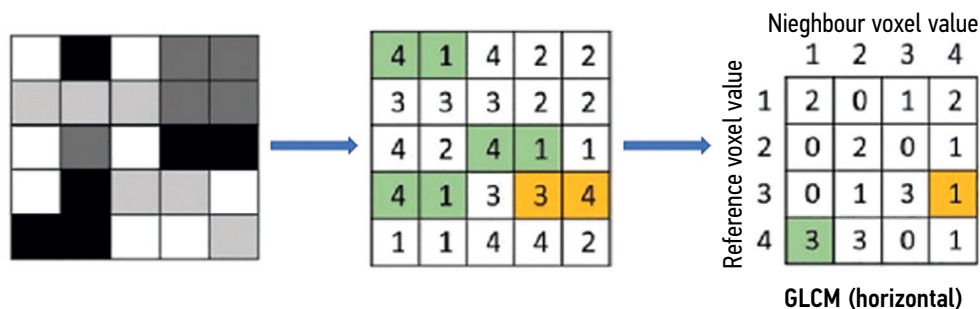


图2. GLCM矩阵指数计算示例: 强度等级为4和1的相邻像素出现了3次 (以绿色标出)。

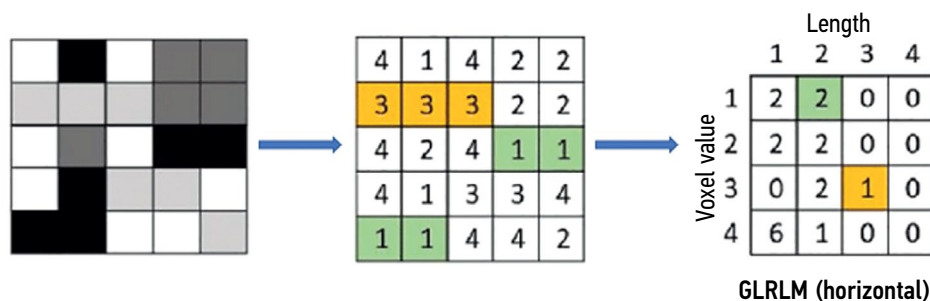


图3. GLRLM指数计算示例: 三个具有相同灰度 (3) 的像素依次出现1次 (以橙色标出)。

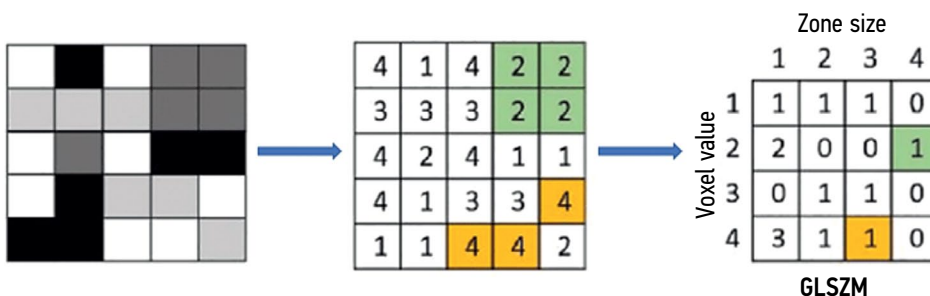


图4. GLSZM指数计算示例: 由4个灰度等于2的像素组成的区域出现1次 (以绿色标出)。

在科学出版物中首次提及“剂量组学”一词要追溯到2018年，H. S. Gabry等人在他们的研究[26]中使用了这种方法来预测153名头颈部癌症患者的口干症发展情况。所有患者都接受了放疗。

得出剂量组学指数的过程包括两个步骤。

1. 三维放射治疗计划使用一系列平行的X射线CT扫描，每次扫描的解剖结构和计划目标体积都由人工或计划系统中的自动数学划定程序确定[27, 28]。
2. 获得三维剂量分布模型后，使用Python编程语言的开源将放射组学掩膜叠加到模型上，并计算出感兴趣区域的定量纹理特征。从剂量分布模型中提取的这些指数被称为剂量组学指数，即上文所述的纹理特征（一阶统计量、邻接矩阵和均匀矩阵）。

在L. Rossi等人的研究[29]中对直肠区域辐射剂量分布的三维模型进行了纹理分析。在绘制辐射剂量分布图后，将放射组学掩膜叠加到感兴趣区域上，并进一步提取纹理特征。图5给出从感兴趣区中提取的剂量组学指数。

由于所研究的数据集通常具有输入变量数量过多的特点，因此出现降低特征空间维度的问题。最常用的特征数与观测值比例规则之一是20 EPV规则。EPV (events per variable) 是指每个独立变量对应的事件发生例数，即较小分组中的患者数除以开发预测模型时考虑的输入特征数[30]。

下一步是通过以下几种方法之一降低特征空间的维度：如主成分分析、线性判别分析、随机森林分析 (Importance函数) 等[31, 32]。然

后，有必要排除高度相关的值，并使用机器学习方法在这些值的基础上构建决定性规则[18]。在最后阶段中，根据研究任务选择预测模型，进行多元统计分析。二元分类模型的准确度通常是通过接受者操作特征曲线 (receiver operating characteristic, ROC) 评估的，在研究中被称为AUC (Area Under the Curve)。该曲线基于灵敏度 (真阳性比例) 和特异度 (真阴性比例)。评价生存模型能力的最常用指数是一致性指数 (C-index)，它是对各个时间点的预测风险指数与观测指数之间的等级相关的指数。该指数基于肯德尔相关系数。

剂量组学在临床实践中的应用

在所分析的国外文献中，可以区分出三个主要的研究方向：(1) 利用剂量组学指数来预测健康组织辐射损伤的发展；(2) 预测肿瘤的复发；(3) 研究剂量组学特征的稳定性和可重复性。此外，还找到了一些文献综述，例如，由R. Sun[33]和X. Zhang[34]领导的作者小组的研究，在这些研究中剂量组学被描述为医学图像纹理分析的一个新方向。

利用剂量组学指数来预测辐射对健康组织的损伤

所有此类研究的共同点是构建预测癌症患者辐射损伤发生率的模型 (规则)。大多数作者的任务是比较基于不同类型数据的预后规则的有效性。这些数据类型包括：临床因素、剂量体积直

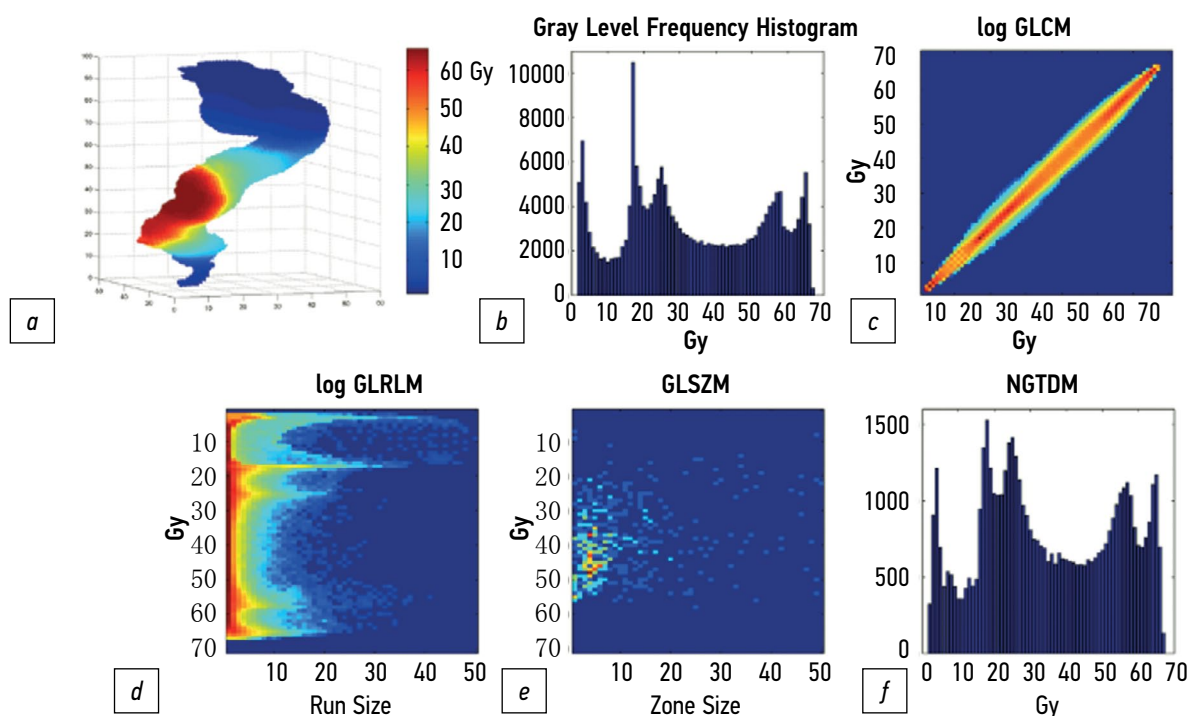


图5. 直肠区域辐射剂量分布三维模型的纹理分析：a——直肠中的三维剂量分布；b——灰度频率直方图；c——GLCM；d——GLRLM；e——GLSZM；f——NGTDM。

方图 (dose - volume histograms, DVH)、肿瘤控制概率 (tumor control probability, TCP) 和正常组织并发症概率 (normal tissue complication probability, NTCP) 的放射生物学模型指数、剂量组学、放射组学和剂量测定指数。

研究人员所使用的指标集、指标组合和统计方法在不同的研究中差别很大。最常见的研究是关于预测接受放疗的癌症患者具有放疗后肺炎的研究。文献显示了, 放疗后肺炎的发病率差异很大 (从5%到58%), 放疗后肺炎是肺癌放疗后最常见的并发症之一[1]。这方面最广泛的研究是Z. Zhang等人在2023年进行的[35]。他们使用了从314名回顾性收集到的肺癌患者数据和35名前瞻性纳入的肺癌患者数据。根据放射组学、剂量组学、剂量体积直方图 (DVH) 的指数和临床因素, 作者构建了模型。决定性规则是通过整合放射组学、剂量组学指数和临床参数而构建的, 它具有最佳的预后能力, 外部测试样本的曲线下面积为0.855 (95%置信区间为0.719-0.990) [35]。根据这项研究的结果, 可以得出结论, 综合不同参数构建的模型具有更高的准确度。

剂量组学和放射组学指数的结合具有最佳的预后能力。这一事实得到了其他研究人员的证实。B. Li等人的研究[36, 37]也具有类似的结果。这项研究的作者从专门分割的肺部功能区中提取指数。Y. Huang等人的研究[2]也具有类似的结果。由L. Zhou等人[38]构建的基于等效辐射剂量分布的模型显示出较高的预后能力, 测试样本的特征曲线下面积为0.799。有趣的是, 在K. M. Kraus等人的研究中[39], 具有相同特征组合但基于吸收辐射剂量分布的预后模型更为有效。这种差异可能与剂量组学指数的可重复性和稳定性问题有关。

一些科学著作对基于剂量测定和剂量组学指数的模型进行了比较。例如, 在由C. Puttanawarut[40]和B. Liang[13, 41]领导的作者小组的研究中, 基于剂量组学指数的模型更为有效。同时, T. Adachi等人的研究结果[42]显示了, 剂量组学和剂量测定指数的结合也具有临床意义。结合放射组学和剂量组学参数的模型不仅在预测放疗后肺炎方面, 而且在预测其他放疗后损伤方面, 例如体重明显减轻 (2个月内超过5%) 方面, 都有很高的准确度。S. H. Lee[43]和P. Han[44]的研究都证实了这一点。因此, P. Han等人在他们的研究中创建了一个医疗决策支持系统。该系统的应用帮助医生提高预测体重明显减轻的准确度。这些研究结果表明, 在临床实践中实施基于剂量组学的决策规则具有现实可能性。X. Zheng等人[45]构建了一个预测肺癌患者急性放射性食管炎模型, 并获得了ROC曲线下面积的最高值 (0.801)。并且他们综合使用了放射组学、剂量组学和临床参数。

W. Ren等人的研究结果[46]表明, 与剂量模型相比, 基于剂量组学指数的决定性规则效率更

高。在这项研究中, 作者预测了确诊为鼻咽癌患者的放射后甲状腺功能减退症的发展情况。在一组诊断类似的患者中, S. S. Yang等人[47]预测了颞叶辐射损伤的发生。基于患者年龄、剂量学和剂量测量参数的模型显示出最佳结果, 外部测试样本的C-index为0.794。

L. Rossi等人的研究[29]结合了临床数据、剂量体积直方图参数和剂量组学指数, 这有助于提高对膀胱和直肠放射治疗晚期并发症 (如夜遗尿、直肠出血、大便失禁) 的预测效果。特别值得关注的是由S. Monti领导的研究[48]。在这项研究中, 作者调查了186名确诊为非小细胞肺癌患者放疗后淋巴细胞减少症的发生、其剂量组学和基因组学指数之间的关系。这些患者接受了化学放疗。作者指出, 所发现的相关性将有助于制定更有效的个体化放疗策略。

所调查的研究结果表明, 将剂量组学指数纳入模型后, ROC曲线下面积增加了。这表明这些指数具有预后价值。

表1给出关于正常组织辐射损伤预测的研究结果。

肿瘤复发/恶化预测

进行这一组研究的一般原则与辐射伤害预测研究不谋而合。因此, 在H. Kamezawa等人[49]和A. Wu[14]的文章中, 预测头颈癌局部复发时基于剂量组学指数的模型最为有效。B. Wang[50]等人也进行了类似的研究。他们利用从CT联合正电子发射断层扫描 (PET-CT) 和放疗计划剂量分布图中提取的纹理指数构建了预测总生存率的模型。综合模型的预测效果优于其他所有模型。

由Y. Murakami[12]和G. Pirrone[51]的作者小组的方法上在前列腺癌复发的预后方面存在一定差异。在第一种情况下, 作者预测了生化复发。他们发现了, 结合临床和剂量测量参数的模型在这项任务中最为有效。在第二种情况下, 局部复发预测模型基于从生物有效剂量分布图、CT和PET-CT图像中提取的放射组学和剂量组学参数。

G. Buizza等人[52]和L. Morelli等人[53]分别证明了剂量测量模型在预测颅底脊索瘤局部复发和骶骨定位方面的有效性。在C. Cai等人的关于预测鼻咽癌复发和转移的研究[54]中, 类似的决定性规则也显示出很高的一致性指数 (C-index)。D. Wang等人[55]的组合模型提出的剂量组学指数表明了, 机器学习在预测放疗后直肠癌完全缓解方面具有潜力。

S. K. Lam等人[56]分析了135名鼻咽癌患者的计算机断层扫描和磁共振图像, 以预测治疗前适应性放疗的可接受性。这项研究的一个特点是使用“轮廓组学”一词, 即一种描述四对感兴趣体积 (volume of interest, VOI) 之间复杂几何关系的方法。基于放射组学的模型准确度最高, 曲线下面积为0.927 (95%置信区间为0.905-0.948)。

表1. 预测辐射对正常组织损伤的研究结果

研究	预测辐射损伤	基于剂量组学模型的AUC	AUC最高的模型
Zhang等人[35]	放疗后肺炎	0.774	R+D+C (AUC=0.855)
Li等人[36]	放疗后肺炎	-	R+Ds (AUC=0.885)
Li等人[37]	放疗后肺炎	0.74	R+D (AUC=0.88)
Huang等人[2]	放疗后肺炎	0.8462	R+D (AUC=0.90)
Zhou等人[38]	放疗后肺炎	-	R+DVH (AUC=0.805)
Kraus等人[39]	放疗后肺炎	0.70	R+D (AUC=0.79)
Puttanawarut等人[40]	放疗后肺炎	0.71	D (AUC=0.71)
Liang等人[13]	放疗后肺炎	0.782	D (AUC=0.782)
Liang等人[41]	放疗后肺炎	0.782	AUC=0.842
Adachi等人[42]	放疗后肺炎	0.837	Ds+D (AUC=0.846)
Lee等人[43]	减肥	-	R+D (AUC=0.710)
Han等人[44]	减肥	-	R+D (准确度=0.73); 医生 (准确度=0.54)
Zheng等人[45]	急性放射性食管炎	0.604	C+R+D (AUC=0.801)
Ren等人[46]	放疗后甲状腺功能减退	0.7	D (AUC=0.7)
Yang等人[47]	颞叶的辐射损伤	-	年龄+DVH+D (C-index=0.794)
Rossi等人[29]	直肠出血	-	C+DVH+D (AUC=0.73)
	大便失禁	-	C+DVH+D (AUC=0.73)
	夜尿	-	C+D (AUC=0.66)
	尿失禁	-	C+DVH+D (AUC=0.73)

注: AUC (area under the curve) ——特征曲线下面积; R——放射组学指数; D——剂量组学指数; Ds——剂量测定指数; C——患者临床数据; DVH (dose - volume histograms) ——剂量体积直方图。

与辐射损伤预后一样, 这组研究结果表明, 基于剂量组学指数的模型具有很高的准确度。表2给出上述关于预测肿瘤复发或恶化的研究结果。

剂量组学特征的可重复性

这组研究中使用的统计模型和方法多种多样。不过, 它们的共同点是剂量组学指数的稳定性和可重复性问题。C. Puttanawarut等人针对这一问题进行了两项研究[57, 58]。在第一项研究中, 作者研究了放射组学和剂量组学指数的普遍性和适用性; 这些指数是通过分析不同定位的肿瘤疾病图像获得的[57]。为此, 研究人员使用了一个数据库, 其中包含101名食道癌患者和93名肺癌患者的数据。作者构建了四个模型来预测诊断为食道癌患者样本的放疗后肺炎的发展, 然后将其应用于肺癌患者样本中的相同目的。在食道癌和肺癌患者样本中, 基于剂量组学和放射组学组合的模型显示出最佳结果, AUC分别为0.75和0.68。这些结果可能表明, 在改变所检查病理的定位时, 决定性规则的应用有限。C. Puttanawarut等人的第二项研究的目的是评估剂量组学指数在模拟剂量分布规划误差时的稳定性[58]。所研究的93个剂量组学指数的类内相关系数 (ICC) 的平均值等于

0.9, 这表明这些指数具有稳定性。不过, 有5个指数的相关系数低于0.75, 这表明了, 其可重复性较低。T. Adachi等人的研究[59]中, 他们也评估了采用不同剂量计算算法时剂量组学指数的可重复性。在所研究的6808个指数中, 34.8%的指数在使用Acuros XB算法时具有较高的可重复性。这表明在使用不同类型的剂量计算时, 剂量组学的应用有限。同时, L. Sun在等人的研究[60]中, 大多数剂量组学特征在剂量计算发生变化时是稳定的。但剂量体积直方图 (DVH) 指数的变异性低于剂量组学特征的。L. Placidi等人[61]确定了四组稳定的剂量组学特征, 以进行进一步研究。在随后的研究中, 作者证明了体素大小在提取剂量组学数据中的重要性[62]。

因此, 指数的规范化、稳定性和可重复性问题仍然是实施此类研究的一个相当重要的方面, 并需要进一步研究。

讨论

在上述研究中, 放疗后肺炎是最常见的预测变量, 共有11项研究。在其中9项研究中, 剂量组学指数被用于构建决定性规则, 而未与其他特

表2. 预测肿瘤恶化的研究结果

研究	预测变量	精确性特性基于剂量组学的模型	精确性特性最佳的模型
Kamezawa等人[49]	头颈部癌局部复发	AUC=0.81	D (AUC=0.81)
Wu等人[14]	头颈部癌局部复发	C-index=0.66	D (C-index=0.66)
Wang等人[50]	头颈部癌局部复发	-	R-PET+R-CT+Ds (C-index=0.873)
Murakami等人[12]	前列腺癌复发	-	D+C (C-index=0.67)
Pirrone等人[51]	前列腺癌复发	AUC=0.68	D (AUC=0.68)
Buizza等人[52]	颅底脊索瘤复发	C-index=0.79	R (C-index=0.80)
Morelli等人[53]	骶骨部位脊索瘤复发	C-index=0.86	D (C-index=0.86)
Cai等人[54]	鼻咽癌的复发和转移	复发的C-index=0.822; 肿瘤转移的C-index=0.786	D (复发的C-index=0.822); D (肿瘤转移的C-index=0.786)
Wang等人[55]	直肠癌缓解	-	AUC=0.828
Lam等人[56]	鼻咽癌放射治疗评估	AUC=0.811	R (AUC=0.927)

注: AUC (area under the curve) ——特征曲线下面积; R——放射组学指数; D——剂量组学指数; Ds——剂量测定指数; C——患者临床数据; PET——正电子发射计算机断层扫描; CT——电子计算机断层扫描。

征相结合。作为此类模型精确性特性的特征曲线下面积 (AUC) 在0.67到0.84之间。基于剂量组学的决定性规则在预测不同部位的肿瘤复发方面也有很高的准确度 (C-index大于0.66)。当构建包括剂量组学、放射组学、剂量测定指数和患者临床数据在内的组合模型时, 精确性特性会增加。这表明该模型具有很高的预后能力, 有望被应用于临床实践, 为患者制定个性化治疗方案。

毫无疑问, 在写本文章时, 由于研究数量少, 样本容量小, 因此需要进一步研究剂量组学及其潜在应用。剂量组学有可能被纳入放疗计划过程。值得注意的是, 在大多数研究中, 剂量组学在与其他定性和定量特征相结合时最为有效。因此, 目前应将剂量组学视为放射组学的有助于提高预后模型效率的一个分支。需要指出的是, 剂量组学和放射组学的指数取决于所使用的软件, 在不同的研究中可能会有很大差异。这些指数的稳定性和可重复性问题是将剂量组学引入临床实践的严重障碍, 需要进一步研究。

结论

因此, 目前剂量组学是放射组学的一个新的有前途的分支, 应用于与癌症患者放射治疗有关的医学

图像的纹理分析。剂量组学可能有助于开发更个性化的放疗计划、预测对正常组织的辐射损伤和诊断复发。

ADDITIONAL INFORMATION

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СПИСОК ЛИТЕРАТУРЫ

- Arroyo-Hernández M., Maldonado F., Lozano-Ruiz F., et al. Radiation-induced lung injury: Current evidence // *BMC Pulm Med*. 2021. Vol. 21, N 1. P. 1–12. doi: 10.1186/s12890-020-01376-4
- Huang Y., Feng A., Lin Y., et al. Radiation pneumonitis prediction after stereotactic body radiation therapy based on 3D dose distribution: Dosiomics and/or deep learning-based radiomics features // *Radiat Oncol*. 2022. Vol. 17, N 1. P. 188. doi: 10.1186/s13014-022-02154-8
- Morelli L., Parrella G., Molinelli S., et al. A dosiomics analysis based on linear energy transfer and biological dose maps to predict local recurrence in sacral chordomas after

- carbon-ion radiotherapy // *Cancers*. 2023. Vol. 15, N 1. P. 33. doi: 10.3390/cancers15010033
4. Ryan S.M., Fingerlin T.E., Mroz M., et al. Radiomic measures from chest high-resolution computed tomography associated with lung function in sarcoidosis // *Eur Respir J*. 2021. Vol. 54, N 2. P. 1900371. doi: 10.1183/13993003.00371-2019
 5. Hooda R., Mittal A., Sofat S. Segmentation of lung fields from chest radiographs: A radiomic feature-based approach // *Biomed Eng Lett*. 2019. Vol. 9, N 1. P. 109–117. doi: 10.1007/s13534-018-0086-z
 6. Zhang B., Ni-Jia-Ti M.Y., Yan R., et al. CT-based radiomics for predicting the rapid progression of coronavirus disease 2019 (COVID-19) pneumonia lesions // *Br J Radiol*. 2021. Vol. 94, N 1122. P. 20201007. doi: 10.1259/bjr.20201007
 7. Avanzo M., Stancanello J., Pirrone G., et al. Radiomics and deep learning in lung cancer // *Strahlenther Onkol*. 2020. Vol. 196, N 10. P. 879–887. doi: 10.1007/s00066-020-01625-9
 8. Ji D., Zhang D., Xu J., et al. Prediction for progression risk in patients with COVID-19 pneumonia: The CALL score // *Clin Infect Dis*. 2020. Vol. 71, N 6. P. 1393–1399. doi: 10.1093/cid/ciaa414
 9. Chen H., Zeng M., Wang X., et al. A CT-based radiomics nomogram for predicting prognosis of coronavirus disease 2019 (COVID-19) radiomics nomogram predicting COVID-19 // *Br J Radiol*. 2021. Vol. 94, N 1117. P. 20200634. doi: 10.1259/bjr.20200634
 10. Wang D., Huang C., Bao S., et al. Study on the prognosis predictive model of COVID-19 patients based on CT radiomics // *Sci Reports*. 2021. Vol. 11, N 1. P. 11591. doi:10.1038/s41598-021-90991-0
 11. Frix A.N., Cousin F., Refaee T., et al. Radiomics in lung diseases imaging: State of the art for clinicians // *J Personal Med*. 2021. Vol. 11, N 7. P. 602. doi: 10.3390/jpm11070602
 12. Murakami Y., Soyano T., Kozuka T., et al. Dose-Based radiomic analysis (dosiomics) for intensity modulated radiation therapy in patients with prostate cancer: Correlation between planned dose distribution and biochemical failure // *Int J Radiat Oncol Biol Phys*. 2022. Vol. 112, N 1. P. 247–259. doi: 10.1016/j.ijrobp.2021.07.1714
 13. Liang B., Yan H., Tian Y., et al. Dosiomics: Extracting 3D spatial features from dose distribution to predict incidence of radiation pneumonitis // *Front Oncol*. 2019. N 9. P. 269. doi: 10.3389/fonc.2019.00269
 14. Wu A., Li Y., Qi M., et al. Dosiomics improves prediction of locoregional recurrence for intensity modulated radiotherapy treated head and neck cancer cases // *Oral Oncol*. 2020. N 104. P. 104625. doi: 10.1016/j.oraloncology.2020.104625
 15. Андреев Д.А., Завьялов А.А. Критерии оценки качества лучевой терапии на примере рака предстательной железы (краткий обзор зарубежной литературы) // *Проблемы социальной гигиены, здравоохранения и истории медицины*. 2021. Т. 29, № S2. С. 1292–1297. doi: 10.32687/0869-866X-2021-29-s2-1292-1297
 16. Chen Q., Xia T., Zhang M., et al. Radiomics in stroke neuroimaging: Techniques, applications, and challenges // *Aging Dis*. 2021. Vol. 12, N 1. P. 143–154. doi: 10.14336/AD.2020.0421
 17. Mayerhoefer M.E., Materka A., Langs G., et al. Introduction to radiomics // *J Nucl Med*. 2020. Vol. 61, N 4. P. 488–495. doi: 10.2967/jnumed.118.222893
 18. Van Timmeren J.E., Cester D., Tanadini-Lang S., et al. Radiomics in medical imaging: “How-to” guide and critical reflection // *Insights Imaging*. 2020. Vol. 11, N 1. P. 91. doi: 10.1186/s13244-020-00887-2
 19. Radiomic Features: pyradiomics v3.0.1.post15+g2791e23 documentation [интернет]. Режим доступа: <https://pyradiomics.readthedocs.io/en/latest/features.html#>. Дата обращения: 21.04.2023.
 20. Al-Areqi F., Konyar M.Z. Effectiveness evaluation of different feature extraction methods for classification of COVID-19 from computed tomography images: A high accuracy classification study // *Biomed Signal Process Control*. 2022. N 76. P. 103662. doi: 10.1016/j.bspc.2022.103662
 21. Zwanenburg A., Vallières M., Abdalah M.A., et al. The image biomarker standardization initiative: Standardized quantitative radiomics for high-throughput image-based phenotyping // *Radiology*. 2020. Vol. 295, N 2. P. 328–338. doi: 10.1148/radiol.2020191145
 22. Galloway M.M. Texture analysis using gray level run lengths // *Comput Graph Image Process*. 1975. Vol. 4, N 2. P. 172–179. doi:10.1016/s0146-664x(75)80008-6
 23. Thibault G., Angulo J., Meyer F. Advanced statistical matrices for texture characterization: application to cell classification // *IEEE Trans Biomed Eng*. 2014. Vol. 61, N 3. P. 630–637. doi: 10.1109/TBME.2013.2284600
 24. Chen S., Harmon S., Perk T., et al. Using neighborhood gray tone difference matrix texture features on dual time point PET/CT images to differentiate malignant from benign FDG-avid solitary pulmonary nodules // *Cancer Imaging*. 2019. Vol. 19, N 1. P. 56. doi: 10.1186/s40644-019-0243-3
 25. He J., Ren J., Niu G., et al. Multiparametric MR radiomics in brain glioma: Models comparison to predict biomarker status // *BMC Med Imaging*. 2022. Vol. 22, N 1. P. 137. doi: 10.1186/s12880-022-00865-8
 26. Gabrys H.S., Buettner F., Sterzing F., et al. Design and selection of machine learning methods using radiomics and dosiomics for normal tissue complication probability modeling of xerostomia // *Front Oncol*. 2018. N 8. P. 35. doi: 10.3389/fonc.2018.00035
 27. Леденев В.В., Нуднов Н.В., Сотников В.М., и др. Результаты количественной оценки постлучевых изменений в легких у онкологических пациентов, полученные с помощью новой методики анализа динамически выполненных РКТ-исследований органов грудной клетки // *Вестник рентгенологии и радиологии*. 2020. Т. 101, № 1. С. 30–38. doi: 10.20862/0042-4676-2020-101-1-30-38
 28. Леденев В.В., Солодкий В.А., Нуднов Н.В., и др. Количественные характеристики лучевого повреждения легочной ткани у онкологических пациентов при лучевой терапии на основании данных РКТ // *Медицинская визуализация*. 2022. Т. 26, № 4. С. 60–74. doi: 10.24835/1607-0763-1182
 29. Rossi L., Bijman R., Schillemans W., et al. Texture analysis of 3D dose distributions for predictive modelling of toxicity rates in radiotherapy // *Radiother Oncol*. 2018. Vol. 129, N 3. P. 548–553. doi: 10.1016/j.radonc.2018.07.027
 30. Liu J., Guo W., Zeng P., et al. Vertebral MRI-based radiomics model to differentiate multiple myeloma from metastases: Influence of features number on logistic regression model performance // *Eur Radiol*. 2021. Vol. 32, N 1. P. 572–581. doi: 10.1007/s00330-021-08150-y
 31. Dhir C.S., Lee S.Y. Discriminant independent component analysis // *IEEE Trans Neural Netw*. 2011. Vol. 22, N 6. P. 845–857. doi: 10.1109/TNN.2011.2122266
 32. Random Forest Feature Importance Computed in 3 Ways with Python / MLJAR [интернет]. Режим доступа: <https://mljar.com/blog/feature-importance-in-random-forest/>. Дата обращения: 21.04.2023.
 33. Sun R., Lerousseau M., Henry T., et al. Intelligence artificielle en radiothérapie: Radiomique, pathomique, et prédiction de la survie et

- de la réponse aux traitements // *Cancer Radiother.* 2021. Vol. 25, N 6-7. P. 630–637. doi: 10.1016/j.canrad.2021.06.027
- 34.** Zhang X., Zhang Y., Zhang G., et al. Deep learning with radiomics for disease diagnosis and treatment: Challenges and potential // *Front Oncol.* 2022. N 12. P. 276. doi: 10.3389/fonc.2022.773840
- 35.** Zhang Z., Wang Z., Yan M., et al. Radiomics and dosiomics signature from whole lung predicts radiation pneumonitis: A model development study with prospective external validation and decision-curve analysis // *Int J Radiat Oncol Biol Phys.* 2023. Vol. 115, N 3. P. 746–758. doi: 10.1016/j.ijrobp.2022.08.047
- 36.** Li B., Ren G., Guo W., et al. Function-Wise Dual-Omics analysis for radiation pneumonitis prediction in lung cancer patients // *Front Pharmacol.* 2022. N 13. P. 3445. doi: 10.3389/fphar.2022.971849
- 37.** Li B., Zheng X., Zhang J., et al. Lung subregion partitioning by incremental dose intervals improves omics-based prediction for acute radiation pneumonitis in non-small-cell lung cancer patients // *Cancers (Basel).* 2022. Vol. 14, N 19. P. 4889. doi: 10.3390/cancers14194889
- 38.** Zhou L., Wen Y., Zhang G., et al. Machine learning-based multiomics prediction model for radiation pneumonitis // *J Oncol.* 2023. Vol. 2023. P. 5328927. doi: 10.1155/2023/5328927
- 39.** Kraus K.M., Oreshko M., Bernhardt D., et al. Dosiomics and radiomics to predict pneumonitis after thoracic stereotactic body radiotherapy and immune checkpoint inhibition // *Front Oncol.* 2023. N 13. P. 1056. doi: 10.3389/fonc.2023.1124592
- 40.** Puttanawarut C., Sirirutbunkajorn N., Khachonkham S., et al. Biological dosiomic features for the prediction of radiation pneumonitis in esophageal cancer patients // *Radiat Oncol.* 2021. Vol. 16, N 1. P. 220. doi: 10.1186/s13014-021-01950-y
- 41.** Liang B., Tian Y., Chen X., et al. Prediction of radiation pneumonitis with dose distribution: A convolutional neural network (CNN) based model // *Front Oncol.* 2020. N 9. P. 1500. doi: 10.3389/fonc.2019.01500
- 42.** Adachi T., Nakamura M., Shintani T., et al. Multi-institutional dose-segmented dosiomic analysis for predicting radiation pneumonitis after lung stereotactic body radiation therapy // *Med Phys.* 2021. Vol. 48, N 4. P. 1781–1791. doi: 10.1002/mp.14769
- 43.** Lee S.H., Han P., Hales R.K., et al. Multi-view radiomics and dosiomics analysis with machine learning for predicting acute-phase weight loss in lung cancer patients treated with radiotherapy // *Phys Med Biol.* 2020. Vol. 65, N 19. P. 195015. doi: 10.1088/1361-6560/ab8531
- 44.** Han P., Lee S.H., Noro K., et al. Improving early identification of significant weight loss using clinical decision support system in lung cancer radiation therapy // *JCO Clin Cancer Inform.* 2021. N 5. P. 944–952. doi: 10.1200/CCI.20.00189
- 45.** Zheng X., Guo W., Wang Y., et al. Multi-omics to predict acute radiation esophagitis in patients with lung cancer treated with intensity-modulated radiation therapy // *Eur J Med Res.* 2023. Vol. 28, N 1. P. 126. doi: 10.1186/s40001-023-01041-6
- 46.** Ren W., Liang B., Sun C., et al. Dosiomics-based prediction of radiation-induced hypothyroidism in nasopharyngeal carcinoma patients // *Phys Medica.* 2021. Vol. 89. P. 219–225. doi: 10.1016/j.ejmp.2021.08.009
- 47.** Yang S.S., OuYang P.Y., Guo J.G., et al. Dosiomics risk model for predicting radiation induced temporal lobe injury and guiding individual intensity-modulated radiation therapy // *Int J Radiat Oncol Biol Phys.* 2023. Vol. 115, N 5. P. 1291–1300. doi: 10.1016/j.ijrobp.2022.11.036
- 48.** Monti S., Xu T., Liao Z., et al. On the interplay between dosiomics and genomics in radiation-induced lymphopenia of lung cancer patients // *Radiother Oncol.* 2022. N 167. P. 219–225. doi: 10.1016/j.radonc.2021.12.038
- 49.** Kamezawa H., Arimura H. Recurrence prediction with local binary pattern-based dosiomics in patients with head and neck squamous cell carcinoma // *Phys Eng Sci Med.* 2022. Vol. 46, N 1. P. 99–107. doi: 10.1007/s13246-022-01201-8
- 50.** Wang B., Liu J., Zhang X., et al. Prognostic value of 18F-FDG PET/CT-based radiomics combining dosiomics and dose volume histogram for head and neck cancer // *EJNMMI Res.* 2023. Vol. 13, N 1. P. 14. doi: 10.1186/s13550-023-00959-6
- 51.** Pirrone G., Matrone F., Chiovati P., et al. Predicting local failure after partial prostate re-irradiation using a dosiomic-based machine learning model // *J Pers Med.* 2022. Vol. 12, N 9. P. 1491. doi: 10.3390/jpm12091491
- 52.** Buizza G., Paganelli C., D'Ippolito E., et al. Radiomics and dosiomics for predicting local control after carbon-ion radiotherapy in skull-base chordoma // *Cancers.* 2021. Vol. 13, N 2. P. 339. doi: 10.3390/cancers13020339
- 53.** Morelli L., Parrella G., Molinelli S., et al. A Dosiomics analysis based on linear energy transfer and biological dose maps to predict local recurrence in sacral chordomas after carbon-ion radiotherapy // *Cancers (Basel).* 2023. Vol. 15, N 1. P. 33. doi: 10.3390/cancers15010033
- 54.** Cai C., Lv W., Chi F., et al. Prognostic generalization of multi-level CT-dose fusion dosiomics from primary tumor and lymph node in nasopharyngeal carcinoma // *Med Phys.* 2023. Vol. 50, N 2. P. 922–934. doi: 10.1002/mp.16044
- 55.** Wang D., Lee S.H., Geng H., et al. Interpretable machine learning for predicting pathologic complete response in patients treated with chemoradiation therapy for rectal adenocarcinoma // *Front Artif Intell.* 2022. N 5. P. 1059033. doi: 10.3389/frai.2022.1059033
- 56.** Lam S.K., Zhang Y., Zhang J., et al. Multi-Organ omics-based prediction for adaptive radiation therapy eligibility in nasopharyngeal carcinoma patients undergoing concurrent chemoradiotherapy // *Front Oncol.* 2022. N 11. P. 792024. doi: 10.3389/fonc.2021.792024
- 57.** Puttanawarut C., Sirirutbunkajorn N., Tawong N., et al. Radiomic and dosiomic features for the prediction of radiation pneumonitis across esophageal cancer and lung cancer // *Front Oncol.* 2022. N 12. P. 768152. doi: 10.3389/fonc.2022.768152
- 58.** Puttanawarut C., Sirirutbunkajorn N., Tawong N., et al. Impact of interfractional error on dosiomic features // *Front Oncol.* 2022. N 12. P. 726896. doi: 10.3389/fonc.2022.726896
- 59.** Adachi T., Nakamura M., Kakino R., et al. Dosiomic feature comparison between dose-calculation algorithms used for lung stereotactic body radiation therapy // *Radiol Phys Technol.* 2022. Vol. 15, N 1. P. 63–71. doi: 10.1007/s12194-022-00651-9
- 60.** Sun L., Smith W., Kirkby C. Stability of dosiomic features against variations in dose calculation: An analysis based on a cohort of prostate external beam radiotherapy patients // *J Appl Clin Med Phys.* 2023. Vol. 24, N 5. P. e13904. doi: 10.1002/acm2.13904
- 61.** Placidi L., Gioscio E., Garibaldi C., et al. A multicentre evaluation of dosiomics features reproducibility, stability and sensitivity // *Cancers (Basel).* 2021. Vol. 13, N 15. P. 3835. doi: 10.3390/cancers13153835
- 62.** Placidi L., Cusumano D., Lenkiewicz J., et al. On dose cube pixel spacing pre-processing for features extraction stability in dosiomic studies // *Phys Medica.* 2021. N 90. P. 108–114. doi: 10.1016/j.ejmp.2021.09.010

REFERENCES

- Arroyo-Hernández M, Maldonado F, Lozano-Ruiz F, et al. Radiation-induced lung injury: Current evidence. *BMC Pulm Med*. 2021;21(1):9. doi: 10.1186/s12890-020-01376-4
- Huang Y, Feng A, Lin Y, et al. Radiation pneumonitis prediction after stereotactic body radiation therapy based on 3D dose distribution: Dosiomics and/or deep learning-based radiomics features. *Radiat Oncol*. 2022;17(1):188. doi: 10.1186/s13014-022-02154-8
- Morelli L, Parrella G, Molinelli S, et al. A dosiomics analysis based on linear energy transfer and biological dose maps to predict local recurrence in sacral chordomas after carbon-ion radiotherapy. *Cancers (Basel)*. 2022;15(1):33. doi: 10.3390/cancers15010033
- Ryan SM, Fingerlin TE, Mroz M, et al. Radiomic measures from chest high-resolution computed tomography associated with lung function in sarcoidosis. *Eur Respir J*. 2019;54(2):1900371. doi: 10.1183/13993003.00371-2019
- Hooda R, Mittal A, Sofat S. Segmentation of lung fields from chest radiographs: A radiomic feature-based approach. *Biomed Eng Lett*. 2018;9(1):109–117. doi: 10.1007/s13534-018-0086-z
- Zhang B, Ni-Jia-Ti MY, Yan R, et al. CT-based radiomics for predicting the rapid progression of coronavirus disease 2019 (COVID-19) pneumonia lesions. *Br J Radiol*. 2021;94(1122):20201007. doi: 10.1259/bjr.20201007
- Avanzo M, Stancanello J, Pirrone G, et al. Radiomics and deep learning in lung cancer. *Strahlenther Onkol*. 2020;196(10):879–887. doi: 10.1007/s00066-020-01625-9
- Ji D, Zhang D, Xu J, et al. Prediction for progression risk in patients with COVID-19 pneumonia: The CALL score. *Clin Infect Dis*. 2020;71(6):1393–1399. doi: 10.1093/cid/ciaa414
- Chen H, Zeng M, Wang X, et al. A CT-based radiomics nomogram for predicting prognosis of coronavirus disease 2019 (COVID-19) radiomics nomogram predicting COVID-19. *Br J Radiol*. 2021;94(1117):20200634. doi: 10.1259/bjr.20200634
- Wang D, Huang C, Bao S, et al. Study on the prognosis predictive model of COVID-19 patients based on CT radiomics. *Sci Rep*. 2021;11(1):11591. doi: 10.1038/s41598-021-90991-0
- Frix AN, Cousin F, Refaee T, et al. Radiomics in lung diseases imaging: State of the Art for Clinicians. *J Pers Med*. 2021;11(7):602. doi: 10.3390/jpm11070602
- Murakami Y, Soyano T, Kozuka T, et al. Dose-Based radiomic analysis (dosiomics) for intensity modulated radiation therapy in patients with prostate cancer: Correlation between planned dose distribution and biochemical failure. *Int J Radiat Oncol Biol Phys*. 2022;112(1):247–259. doi: 10.1016/j.ijrobp.2021.07.1714
- Liang B, Yan H, Tian Y, et al. Dosiomics: Extracting 3D spatial features from dose distribution to predict incidence of radiation pneumonitis. *Front Oncol*. 2019;(9):269. doi: 10.3389/fonc.2019.00269
- Wu A, Li Y, Qi M, et al. Dosiomics improves prediction of locoregional recurrence for intensity modulated radiotherapy treated head and neck cancer cases. *Oral Oncol*. 2020;(104):104625. doi: 10.1016/j.oraloncology.2020.104625
- Andreev DA, Zavyalov AA. The quality indicators to assess the prostate cancer radiotherapy performance (brief review). *Problems Social Hygiene Public Health History Med*. 2021;29(S2):1292–1297. (In Russ). doi: 10.32687/0869-866X-2021-29-s2-1292-1297
- Chen Q, Xia T, Zhang M, et al. Radiomics in stroke neuroimaging: Techniques, applications, and challenges. *Aging Dis*. 2021;12(1):143–154. doi: 10.14336/AD.2020.0421
- Mayerhoefer ME, Materka A, Langs G, et al. Introduction to radiomics. *J Nucl Med*. 2020;61(4):488–495. doi: 10.2967/jnumed.118.222893
- Van Timmeren JE, Cester D, Tanadini-Lang S, et al. Radiomics in medical imaging: “How-to” guide and critical reflection. *Insights Imaging*. 2020;11(1):91. doi: 10.1186/s13244-020-00887-2
- Radiomic Features — pyradiomics v3.0.1.post15+g2791e23 documentation [Internet]. Available from: <https://pyradiomics.readthedocs.io/en/latest/features.html#>. Accessed: 21.04.2023.
- Al-Areqi F, Konyar MZ. Effectiveness evaluation of different feature extraction methods for classification of COVID-19 from computed tomography images: A high accuracy classification study. *Biomed Signal Process Control*. 2022;(76):103662. doi: 10.1016/j.bspc.2022.103662
- Zwanenburg A, Vallières M, Abdalah MA, et al. The image biomarker standardization initiative: Standardized quantitative radiomics for high-throughput image-based phenotyping. *Radiology*. 2020;295(2):328–338. doi: 10.1148/radiol.2020191145
- Galloway MM. Texture analysis using gray level run lengths. *Comput Graph Image Process*. 1975;4(2):172–179. doi: 10.1016/S0146-664X(75)80008-6
- Thibault G, Angulo J, Meyer F. Advanced statistical matrices for texture characterization: Application to cell classification. *IEEE Trans Biomed Eng*. 2014;61(3):630–637. doi: 10.1109/TBME.2013.2284600
- Chen S, Harmon S, Perk T, et al. Using neighborhood gray tone difference matrix texture features on dual time point PET/CT images to differentiate malignant from benign FDG-avid solitary pulmonary nodules. *Cancer Imaging*. 2019;19(1):56. doi: 10.1186/s40644-019-0243-3
- He J, Ren J, Niu G, et al. Multiparametric MR radiomics in brain glioma: Models comparison to predict biomarker status. *BMC Med Imaging*. 2022;22(1):137. doi: 10.1186/s12880-022-00865-8
- Gabryś HS, Buettner F, Sterzing F, et al. Design and selection of machine learning methods using radiomics and dosiomics for normal tissue complication probability modeling of xerostomia. *Front Oncol*. 2018;8:35. doi: 10.3389/fonc.2018.00035
- Ledenev VV, Nudnov NV, Sotnikov VM, et al. The results of quantitative evaluation of postradiation changes in lung cancer patients, which were obtained using a new procedure for analysis of dynamic X-ray computed tomography imaging of thoracic organs. *J Radiol Nuclear Med*. 2020;101(1):30–38. (In Russ). doi: 10.20862/0042-4676-2020-101-1-30-38
- Ledenev VV, Solodkiy VA, Nudnov NV, et al. Quantitative characteristics of radiation-induced lung damage in oncological patients during radiotherapy based on RCT data. *Med Visual*. 2022;26(4):60–74. (In Russ). doi: 10.24835/1607-0763-1182
- Rossi L, Bijman R, Schillemans W, et al. Texture analysis of 3D dose distributions for predictive modelling of toxicity rates in radiotherapy. *Radiother Oncol*. 2018;129(3):548–553. doi: 10.1016/j.radonc.2018.07.027
- Liu J, Guo W, Zeng P, et al. Vertebral MRI-based radiomics model to differentiate multiple myeloma from metastases: Influence of features number on logistic regression model performance. *Eur Radiol*. 2022;32(1):572–581. doi: 10.1007/s00330-021-08150-y

31. Dhir CS, Lee SY. Discriminant independent component analysis. *IEEE Trans Neural Netw*. 2011;22(6):845–857. doi: 10.1109/TNN.2011.2122266
32. Random Forest Feature Importance Computed in 3 Ways with Python | MLJAR [Internet]. Available from: <https://mljar.com/blog/feature-importance-in-random-forest/>. Accessed: 21.04.2023.
33. Sun R, Lerousseau M, Henry T, et al. Intelligence artificielle en radiothérapie: Radiomique, pathomique, et prédiction de la survie et de la réponse aux traitements. *Cancer Radiother*. 2021;25(6-7):630–637. doi: 10.1016/j.canrad.2021.06.027
34. Zhang X, Zhang Y, Zhang G, et al. Deep learning with radiomics for disease diagnosis and treatment: challenges and potential. *Front Oncol*. 2022;(12):773840. doi: 10.3389/fonc.2022.773840
35. Zhang Z, Wang Z, Yan M, et al. Radiomics and dosiomics signature from whole lung predicts radiation pneumonitis: A model development study with prospective external validation and decision-curve analysis. *Int J Radiat Oncol Biol Phys*. 2023;115(3):746–758. doi: 10.1016/j.ijrobp.2022.08.047
36. Li B, Ren G, Guo W, et al. Function-Wise dual-omics analysis for radiation pneumonitis prediction in lung cancer patients. *Front Pharmacol*. 2022;(13):971849. doi: 10.3389/fphar.2022.971849
37. Li B, Zheng X, Zhang J, et al. Lung subregion partitioning by incremental dose intervals improves omics-based prediction for acute radiation pneumonitis in non-small-cell lung cancer patients. *Cancers (Basel)*. 2022;14(19):4889. doi: 10.3390/cancers14194889
38. Zhou L, Wen Y, Zhang G, et al. Machine learning-based multiomics prediction model for radiation pneumonitis. *J Oncol*. 2023;2023:5328927. doi: 10.1155/2023/5328927
39. Kraus KM, Oreshko M, Bernhardt D, et al. Dosiomics and radiomics to predict pneumonitis after thoracic stereotactic body radiotherapy and immune checkpoint inhibition. *Front Oncol*. 2023;(13):1124592. doi: 10.3389/fonc.2023.1124592
40. Puttanawarut C, Sirirutbunkajorn N, Khachonkham S, et al. Biological dosiomic features for the prediction of radiation pneumonitis in esophageal cancer patients. *Radiat Oncol*. 2021;16(1):220. doi: 10.1186/s13014-021-01950-y
41. Liang B, Tian Y, Chen X, et al. Prediction of radiation pneumonitis with dose distribution: A convolutional neural network (CNN) based model. *Front Oncol*. 2020;(9):1500. doi: 10.3389/fonc.2019.01500
42. Adachi T, Nakamura M, Shintani T, et al. Multi-institutional dose-segmented dosiomic analysis for predicting radiation pneumonitis after lung stereotactic body radiation therapy. *Med Phys*. 2021;48(4):1781–1791. doi: 10.1002/mp.14769
43. Lee SH, Han P, Hales RK, et al. Multi-view radiomics and dosiomics analysis with machine learning for predicting acute-phase weight loss in lung cancer patients treated with radiotherapy. *Phys Med Biol*. 2020;65(19):195015. doi: 10.1088/1361-6560/ab8531
44. Han P, Lee SH, Noro K, et al. Improving early identification of significant weight loss using clinical decision support system in lung cancer radiation therapy. *JCO Clin Cancer Inform*. 2021;(5):944–952. doi: 10.1200/CCI.20.00189
45. Zheng X, Guo W, Wang Y, et al. Multi-omics to predict acute radiation esophagitis in patients with lung cancer treated with intensity-modulated radiation therapy. *Eur J Med Res*. 2023;28(1):126. doi: 10.1186/s40001-023-01041-6
46. Ren W, Liang B, Sun C, et al. Dosiomics-based prediction of radiation-induced hypothyroidism in nasopharyngeal carcinoma patients. *Phys Med*. 2021;(89):219–225. doi: 10.1016/j.ejmp.2021.08.009
47. Yang SS, OuYang PY, Guo JG, et al. Dosiomics risk model for predicting radiation induced temporal lobe injury and guiding individual intensity-modulated radiation therapy. *Int J Radiat Oncol Biol Phys*. 2023;115(5):1291–1300. doi: 10.1016/j.ijrobp.2022.11.036
48. Monti S, Xu T, Liao Z, et al. On the interplay between dosiomics and genomics in radiation-induced lymphopenia of lung cancer patients. *Radiother Oncol*. 2022;(167):219–225. doi: 10.1016/j.radonc.2021.12.038
49. Kamezawa H, Arimura H. Recurrence prediction with local binary pattern-based dosiomics in patients with head and neck squamous cell carcinoma. *Phys Eng Sci Med*. 2023;46(1):99–107. doi: 10.1007/s13246-022-01201-8
50. Wang B, Liu J, Zhang X, et al. Prognostic value of 18F-FDG PET/CT-based radiomics combining dosiomics and dose volume histogram for head and neck cancer. *EJNMMI Res*. 2023;13(1):14. doi: 10.1186/s13550-023-00959-6
51. Pirrone G, Matrone F, Chiovati P, et al. Predicting local failure after partial prostate re-irradiation using a dosiomic-based machine learning model. *J Pers Med*. 2022;12(9):1491. doi: 10.3390/jpm12091491
52. Buizza G, Paganelli C, D'Ippolito E, et al. Radiomics and dosiomics for predicting local control after carbon-ion radiotherapy in skull-base chordoma. *Cancers (Basel)*. 2021;13(2):339. doi: 10.3390/cancers13020339
53. Morelli L, Parrella G, Molinelli S, et al. A dosiomics analysis based on linear energy transfer and biological dose maps to predict local recurrence in sacral chordomas after carbon-ion radiotherapy. *Cancers (Basel)*. 2022;15(1):33. doi: 10.3390/cancers15010033
54. Cai C, Lv W, Chi F, et al. Prognostic generalization of multi-level CT-dose fusion dosiomics from primary tumor and lymph node in nasopharyngeal carcinoma. *Med Phys*. 2023;50(2):922–934. doi: 10.1002/mp.16044
55. Wang D, Lee SH, Geng H, et al. Interpretable machine learning for predicting pathologic complete response in patients treated with chemoradiation therapy for rectal adenocarcinoma. *Front Artif Intell*. 2022;(5):1059033. doi: 10.3389/frai.2022.1059033
56. Lam SK, Zhang Y, Zhang J, et al. Multi-Organ omics-based prediction for adaptive radiation therapy eligibility in nasopharyngeal carcinoma patients undergoing concurrent chemoradiotherapy. *Front Oncol*. 2022;(11):792024. doi: 10.3389/fonc.2021.792024
57. Puttanawarut C, Sirirutbunkajorn N, Tawong N, et al. Radiomic and dosiomic features for the prediction of radiation pneumonitis across esophageal cancer and lung cancer. *Front Oncol*. 2022;(12):768152. doi: 10.3389/fonc.2022.768152
58. Puttanawarut C, Sirirutbunkajorn N, Tawong N, et al. Impact of interfractional error on dosiomic features. *Front Oncol*. 2022;(12):726896. doi: 10.3389/fonc.2022.726896
59. Adachi T, Nakamura M, Kakino R, et al. Dosiomic feature comparison between dose-calculation algorithms used for lung stereotactic body radiation therapy. *Radiol Phys Technol*. 2022;15(1):63–71. doi: 10.1007/s12194-022-00651-9
60. Sun L, Smith W, Kirkby C. Stability of dosiomic features against variations in dose calculation: An analysis based on a cohort of

prostate external beam radiotherapy patients. *J Appl Clin Med Phys*. 2023;24(5):e13904. doi: 10.1002/acm2.13904

61. Placidi L, Gioscio E, Garibaldi C, et al. A Multicentre evaluation of dosiomics features reproducibility, stability and sensitivity. *Cancers (Basel)*. 2021;13(15):3835. doi: 10.3390/cancers13153835

62. Placidi L, Cusumano D, Lenkowicz J, et al. On dose cube pixel spacing pre-processing for features extraction stability in dosiomic studies. *Phys Med*. 2021;(90):108–114. doi: 10.1016/j.ejmp.2021.09.010

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