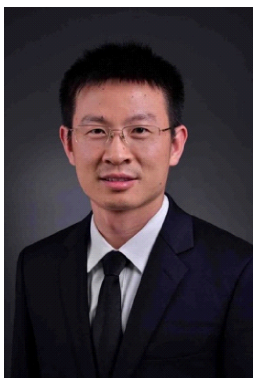


· 学术前沿 ·

甲状腺微小乳头状癌消融治疗的现状及进展

陈夏怡, 周玲燕, 陈晨, 隋琳, 闫玉琪, 徐栋

浙江省肿瘤医院 中国科学院杭州医学研究所, 浙江 杭州 310022



徐栋教授, 医学博士, 主任医师, 博士生导师, 中国科学院大学附属肿瘤医院(浙江省肿瘤医院)党委委员、超声医学科主任, 台州院区党委书记, 浙江省卫生高层次领军人才, 美国 MD Anderson 癌症中心客座教授。现任中国医师协会介入医师分会超声介入专委会主任委员, 中国抗癌协会肿瘤消融治疗专委会副主任委员, 中华医学会超声医学分会委员, 中国医师协会介入医师分会常委, 浙江省医学会超声医学分会候任主任委员, 浙江省抗癌协会肿瘤消融治疗专委会主任委员, 浙江省数理医学学会精准超声介入与智能诊断专委会主任委员等。主持多项国家自然科学基金及浙江省自然科学基金重大项目, 在 SCI 杂志及国内核心期刊发表论文上百篇, 牵头制定了甲状腺微创消融治疗专家共识等多项国际国内指南共识, 主编了人民卫生出版社教材《甲状腺肿瘤消融治疗》等多部医学著作。

摘要: 随着消融技术的不断发展, 消融已成为甲状腺微小乳头状癌(PTMC)的一种新的治疗选择。近年来有多项临床研究探讨各种消融技术治疗 PTMC 的可行性、安全性和长期疗效。本文针对近期 PTMC 消融治疗手段及其疗效进行综述, 旨在为该疾病的治疗和方案选择提供参考。

关键词: 甲状腺微小乳头状癌; 热消融治疗; 射频消融; 微波消融; 激光消融; 高强度聚焦超声; 不可逆电穿孔
中图分类号: R734.2 **文献标识码:** A **文章编号:** 1674-8182(2023)11-1613-06

Recent status and advances of ablation for papillary thyroid microcarcinoma

CHEN Xiayi, ZHOU Lingyan, CHEN Chen, SUI Lin, YAN Yuqi, XU Dong

Zhejiang Cancer Hospital, Hangzhou Institute of Medicine (HIM), Chinese Academy of Sciences, Hangzhou, Zhejiang 310022, China

Corresponding author: XU Dong, E-mail: xudong@zjcc.org.cn

Abstract: With the continuous development of ablation technology, ablation has become a new treatment option for papillary thyroid microcarcinoma (PTMC). Numerous clinical studies have been carried out recently to confirm the viability, safety, and long-term effectiveness of different ablation procedures in the treatment of PTMC. In order to give the most up-to-date information and treatment choices for PTMC, this article examines current ablation therapy options for PTMC and their effectiveness.

Keywords: Papillary thyroid microcarcinoma; Thermal ablation therapy; Radio-frequency ablation; Microwave ablation; Laser ablation; High-intensity focused ultrasound; Irreversible electroporation

1 消融治疗的概述

甲状腺乳头状癌的发病率呈逐年上升趋势, 其中肿瘤最大直径 ≤ 1 cm 的甲状腺微小乳头状癌(papillary thyroid microcarcinoma, PTMC)的占比已超过

50%^[1-2]。PTMC 属于惰性癌症类型, 生长缓慢, 不易转移和侵犯^[3]。

自 2009 年美国甲状腺协会发布的分化型甲状腺癌管理指南中首次提及了射频消融后^[4], 2015 年中国发布了甲状腺良性结节、微小癌及颈部转移性淋巴

结热消融治疗的浙江省专家共识^[5],共识中明确提出热消融治疗甲状腺相关疾病的具体临床规范,并于 2018 年发布中国共识^[6],进一步规范热消融技术在甲状腺肿瘤中的应用;次年,中国临床肿瘤学会发布指南提出甲状腺癌的消融适应证局限于 3~4 个病灶且直径 $<2\text{ cm}$ ^[7];2020 年日本发布的有关 PTMC 主动监测的共识中未提及热消融技术^[8];2021 年欧洲甲状腺协会发布了消融治疗恶性甲状腺病变的指南^[9];2022 年美国、英国、欧洲、意大利、韩国等多个国家发布消融治疗甲状腺良恶性疾病的联合共识,对不同消融技术的原理、疗效进行详细介绍^[10]。目前为止,所有指南和共识均指出 PTMC 的一线治疗方法为外科手术,然而长期研究发现外科手术的术中风险和术后并发症的发生率较高,患者满意度普遍较低^[11-12]。因此随访观察或消融治疗为 PTMC 提供了新的治疗选择^[6,9,13-15]。

消融技术分为热消融和非热消融,本文主要围绕热消融中的射频消融(radio-frequency ablation, RFA)、微波消融(microwave ablation, MWA)、激光消融(laser ablation, LA)和高强度聚焦超声(high-intensity focused ultrasound, HIFU)以及非热消融中的不可逆电穿孔(irreversible electroporation, IRE)展开描述。热消融的主要作用原理是基于极端高温条件下对组织造成不可逆性损伤^[10]。而 IRE 的作用机制是短时间内利用强大的电场脉冲在细胞膜上留下永久性的渗透作用,从而破坏细胞活性^[16]。由于消融治疗具有对周围组织创伤小、术后恢复时间短及切口美观等特点,近年来被广泛用于治疗低危 PTMC^[17]。

2 PTMC 消融的治疗方案

2.1 术前评估 消融是一种在原位灭活肿瘤并达到局部根治的技术,其对肿瘤以及患者自身的要求较高,因此消融前的详细检查以及评估至关重要。患者术前需进行超声检查以确定肿瘤大小、位置、回声、囊实性成分和血管供应情况,以便选择最佳的消融技术^[10,18]。此外,为了避免对患者的过度治疗,术前均需进行穿刺活检(推荐使用细针穿刺活检行细胞学检查)以明确病理类型^[6]。

2.2 热消融技术

2.2.1 RFA RFA 作为 PTMC 的常用消融治疗方法之一,其独特作用原理在于通过释放射频电流搅动组织离子产生热效应^[19],使整个靶区的温度达到 50~100℃并维持 4~6 min,从而发生不可逆的细胞损伤以及近距离组织凝固^[10]。

Yan 等^[20]对 884 例 PTMC 患者开展研究,其中 460 例患者接受传统外科手术,424 例患者进行 RFA 治疗,经过平均 48.3 个月的随访,结果显示与传统手术组相比,接受 RFA 患者的手术时间较短、术中失血量较少、住院时间较短、治疗成本较低,且术后并发症发生率低。一项包括 15 个研究的荟萃分析显示,1 770 例接受 RFA 治疗的 PTMC 患者的肿瘤完全消失率为 79% (95% CI: 65%~94%),平均随访时间 33.0 个月,肿瘤进展率为 1.5%,仅 0.9% 的患者出现新的病灶,0.2% 出现淋巴结转移^[21]。一项随访时间超过 5 年的回顾性研究发现,RFA 治疗 PTMC 的术后体积缩小率达到 $(100\pm 0.3)\%$,且 96.9% 的肿瘤病灶消失,没有患者出现并发症或延迟手术^[22]。Li 等^[23]研究 RFA 治疗对后续手术管理的影响,对 10 例接受 RFA 治疗后因担心 RFA 新技术的疗效以及缺乏家庭支持等因素再次接受外科手术的 PTMC 患者开展研究,术中可见所有患者未出现肌肉和神经损伤,且病理检查未发现残留病灶。因此,如有必要,RFA 并不影响后续手术管理。此外,Scappaticcio 等^[24]对接受 RFA 的 PTMC 患者术后动态风险分层系统进行进一步评估,将患者分为完全、不确定或不完全应答三类,这一应答系统可以有效预测肿瘤的进展风险并可及时调整随访计划。

近年有研究比较 RFA 和外科手术治疗 $T_{1b}N_0M_0$ (肿瘤最大直径 $>1\sim 2\text{ cm}$) 甲状腺乳头状癌的疗效,结果显示在局部肿瘤进展、淋巴结转移、肿瘤复发、无复发生存率等方面差异无统计学意义,且 RFA 在治疗时间、手术成本、术中失血量和术后并发症方面表现良好^[15,25-26]。Tang 等^[27]对 559 例发生颈部淋巴结转移的 PTMC 患者进行的荟萃分析显示,接受 RFA 治疗的肿瘤体积缩小率达到了 95.57%,手术并发症发生率为 0.3%。Song 等^[28]对峡部 PTMC 患者进行 RFA 治疗,1、3、6、12 和 18 个月的消融区消失率为 0.8%、10.4%、51.3%、90.4% 和 100%,且没有患者出现远处转移。现有甲状腺乳头状癌的消融适应指征将在大量临床研究和探索中有望得到扩展和更新。

但 RFA 也存在一定局限性,对于妊娠期或体内有植入式心律转复除颤器(ICD)患者,可能存在胎儿损伤或影响 ICD 功能的问题^[10]。期待未来有系统培训的操作课程供临床医生学习以提高实践水平。最后,结合近年来多项临床研究结果证实 RFA 对低风险 PTMC 具有良好的疗效,可以为不耐受或拒绝手术的患者提供一种新的微创治疗方案^[10-11, 29-32]。

2.2.2 MWA MWA 能够利用介质滞后产生大量热

量,当组织被电磁场产生的致命热量破坏时,组织中的极性分子(尤其是水分)被迫增加动能以提高组织温度^[33]。基于辐射特性,MWA能较为轻易地穿透并加热周围聚集的组织(无论烧焦或干燥),从而突破传输功率有限这一局限性^[34]。此外,MWA还可以利用热协同效应同时处理多个肿瘤,且在激活过程中连续供电,从而做到有效加热^[35]。

一项长达5年的随访报告指出MWA治疗后所有肿瘤均完全消失,体积缩小率为(99.37±4.02)%,且术后均未发生复发、淋巴结转移或远处转移^[36]。Wei等^[37]对1029例接受MWA或外科手术的PTMC患者开展研究发现,MWA的术中失血量和手术用时较少,重大并发症的发生率为5.4%,且所有MWA组患者术后均未发生永久性声音嘶哑。最新的荟萃分析表明与传统手术相比,MWA能够成为一种有效、安全的PTMC治疗方案^[38]。为了更好地验证MWA的疗效,病理组织学科也开展了一系列的研究,研究结果显示MWA术后病理检查中容易见到成纤维细胞增生或慢性炎症^[39],且均未见残留肿瘤组织^[40]。另外,MWA术后部分促炎症和肿瘤作用的基因表达发生下调^[41]。

目前MWA仍局限于治疗单灶性PTMC,因此国内外开始探索MWA对多灶性PTMC的疗效。多项研究表明,接受MWA治疗的多灶性PTMC病例均实现完全消融,技术成功率和体积缩小率均达到100%,且术后并发症较少^[42-45]。此外,为了进一步研究MWA对已侵犯包膜的PTMC患者疗效,Zheng等^[45]进行了一项前瞻性研究显示,包膜侵犯组和未侵犯组技术成功率分别为99%和100%,并且两组在疾病进展和肿瘤体积缩小率方面差异无统计学意义。此外,中国学者针对临近被膜、侵犯被膜和位于峡部的PTMC患者开展研究,结果均表明MWA对PTMC的疗效较好^[46-48]。综上所述,MWA是PTMC的一个有效且安全的微创治疗方法。

2.2.3 LA 与其他热消融技术相比,LA能够更加精准地进行穿刺,并且能够控制侧方热扩散,保护周围大血管、气管壁或者喉返神经。LA的技术原理是通过组织吸收光子加热,靠近石英光纤(300~600 μm)尖端进行能量的输出,高温使病变组织汽化,足量的激光能够导致整个目标汽化、碳化或凝固性坏死^[49-50]。因此对于肿瘤靠近关键结构或者体内存有起搏器的PTMC患者仍可适用^[51]。

一项长达10年的回顾性研究发现,PTMC患者对LA的耐受性较好,术后3~10个月所有消融区域

全部消失或出现瘢痕,术后12个月肿瘤消失率为100%。同时,LA术后甲状腺激素和自身抗体水平均未出现明显变化^[52]。Zhou等^[53]研究发现,LA相对于外科手术治疗PTMC的住院时间和手术时间较短,体积缩小率差异无统计学意义。Valcavi等^[54]从病理学和免疫组化方面对LA的疗效研究发现,LA治疗后肿瘤组织会发生失构和碳化,TTF1和抗线粒体抗体表达完全丧失。该结果同样证实了LA治疗PTMC是可行且有效的。为了研究LA对老年PTMC患者的疗效,Juan等^[55]对38例符合要求的PTMC老年患者进行一项为期5年的回顾性研究,结果显示所有老年患者术后均未出现明显的并发症和淋巴结转移,术后4年所有肿瘤完全消失。LA对无法进行手术的PTMC老年患者有效且安全。

早在2013年有学者对颈部淋巴结转移的PTMC患者开展研究,研究发现接受LA治疗的技术成功率为100%,且未见明显手术并发症。近年相关研究也证实了LA是颈部淋巴结转移PTMC患者的一个有效替代方案^[56-57]。Zhang等^[1]研究发现LA对多灶性PTMC患者的疗效相当,该研究对LA治疗单灶性和多灶性PTMC进行对比,结果表明两组体积缩小率差异无统计学意义,所有消融区域均全部消失。由此可见,不符合外科手术的多灶性PTMC患者可以考虑LA治疗。此外,多项研究和共识均证明LA是PTMC的一种安全且有效的治疗方法^[51, 58-60]。

2.2.4 HIFU HIFU是唯一一个完全做到无创消融的技术,它利用声波来瞄准病变部位,将多个声源的高强度声波聚焦到同一个靶点上,能量集中在一个小区域,短时间内产生超过85℃的高温,从而使细胞死亡^[9, 19]。到目前为止,HIFU仅应用于良性甲状腺结节,对PTMC的治疗效果在文献中描述较少,因此仍需要大量临床研究和探索来验证其安全性和有效性。

2.3 IRE IRE是治疗PTMC的一种新兴消融方法,其独特的作用机制是利用高频电场脉冲诱导和跨膜电位使膜发生永久性渗透(即纳米孔),当跨膜电位达到阈值就会出现不可逆的电穿孔^[61-62]。IRE主要诱导细胞凋亡(程序化、受调控的非炎症性细胞死亡),能够避免对大血管、气管组织、周围神经组织和细胞外基质造成损伤^[61-63],与其他消融技术相比,IRE不会产生任何有损害的热效应。同时,IRE所需要的脉冲时间较短暂,消融目标区域界限清晰,因此能较为高效地治疗目标肿瘤^[64]。但是IRE的不足之处在于对操作人员的技术要求比较高,国内尚未有标准化手术操作规范^[63]。此外,现今国产的IRE消融

器材缺乏,导致其治疗费用较为昂贵,造成大部分患者选择受限。

近年来,IRE 在肝脏、胰腺和前列腺肿瘤中的疗效已被多个研究结果证实^[16]。除了用于治疗原发性前列腺癌外,IRE 也成为了复发性前列腺癌的一种挽救性方案^[65]。Bhutiani 等^[66]对 55 例肝细胞癌患者开展研究,将 IRE 和 MWA 的治疗疗效进行比较,发现 IRE 组能够较大程度改善肝脏的耐受性。此外,在治疗胰腺癌的临床应用中,IRE 也展现出了独特的技术优势^[67]。与此同时,由于甲状腺的特殊解剖结构,目前仍需要大量的前瞻性研究来验证 IRE 治疗 PTMC 的安全性和有效性^[62]。浙江省肿瘤医院超声诊疗中心为此开展了一项三期临床试验,现已初步取得较好结果,期待补充更多的随访数据以证实 IRE 对 PTMC 的长期疗效。

3 总结与展望

现今,消融技术日益成熟并呈现出加速发展的趋势,多国开展大量的临床研究以验证其长期疗效和安全性。结合目前大规模的临床研究结果,对于不耐受或者拒绝外科手术的低风险 PTMC 患者,可以根据肿瘤及患者特点来考虑合适的消融技术进行治疗。尽管部分消融技术已在 PTMC 患者中开展,但其规范化系统化治疗仍处于探索和完善阶段。期待未来能建立一个更加完备的 PTMC 消融治疗管理标准,为患者带去更安全更高效更满意的治疗方案。

利益冲突 无

参考文献

- [1] Zhang L, Zhang GP, Zhan W, et al. The feasibility and efficacy of ultrasound-guided percutaneous laser ablation for multifocal papillary thyroid microcarcinoma[J]. *Front Endocrinol (Lausanne)*, 2022, 13: 921812.
- [2] LeClair K, Bell KJL, Furuya-Kanamori L, et al. Evaluation of gender inequity in thyroid cancer diagnosis[J]. *JAMA Intern Med*, 2021, 181(10): 1351.
- [3] Lam AK. Histopathological assessment for papillary thyroid carcinoma[M]// *Papillary Thyroid Carcinoma*. New York: Humana, 2022: 93-108.
- [4] American Thyroid Association (ATA) Guidelines Taskforce on Thyroid Nodules and Differentiated Thyroid Cancer, Cooper DS, Doherty GM, et al. Revised American Thyroid Association management guidelines for patients with thyroid nodules and differentiated thyroid cancer[J]. *Thyroid*, 2009, 19(11): 1167-1214.
- [5] 葛明华,徐栋,杨安奎,等.甲状腺良性结节、微小癌及颈部转移性淋巴结热消融治疗浙江省专家共识(2015 版)[J]. *中国普通外科杂志*, 2016,25(7):944-946.
- [6] 葛明华,徐栋,杨安奎,等.甲状腺良性结节、微小癌及颈部转移性淋巴结热消融治疗专家共识(2018 版)[J]. *中国肿瘤*, 2018, 27(10):768-773.
- [7] 陈立波,丁勇,关海霞,等.中国临床肿瘤学会(CSCO)持续/复发及转移性分化型甲状腺癌诊疗指南-2019[J]. *肿瘤预防与治疗*, 2019,32(12):1051-1080.
- [8] Sugitani I, Ito Y, Takeuchi D, et al. Indications and strategy for active surveillance of adult low-risk papillary thyroid microcarcinoma: consensus statements from the Japan association of endocrine surgery task force on management for papillary thyroid microcarcinoma[J]. *Thyroid*, 2021, 31(2): 183-192.
- [9] Mauri G, Hegedüs L, Bandula S, et al. European thyroid association and cardiovascular and interventional radiological society of Europe 2021 clinical practice guideline for the use of minimally invasive treatments in malignant thyroid lesions[J]. *Eur Thyroid J*, 2021, 10(3): 185-197.
- [10] Orloff LA, Noel JE, Stack BC Jr, et al. Radiofrequency ablation and related ultrasound-guided ablation technologies for treatment of benign and malignant thyroid disease: an international multidisciplinary consensus statement[J]. *Head Neck*, 2022, 44(3): 633-660.
- [11] 冯娜,黄品同,徐栋,等.甲状腺微小乳头状癌射频消融术与外科手术的比较[J]. *介入放射学杂志*, 2021,30(4):356-360.
- [12] Shen KJ, Xue SB, Xie Y, et al. Comparison of thermal ablation and routine surgery for the treatment of papillary thyroid microcarcinoma: a systematic review and Meta-analysis[J]. *Int J Hypertherm*, 2020, 37(1): 913-924.
- [13] 中华医学会内分泌学分会,中华医学会外科学分会甲状腺及代谢外科学组,中国抗癌协会头颈肿瘤专业委员会,等.甲状腺结节和分化型甲状腺癌诊疗指南(第二版)[J]. *中华内分泌代谢杂志*, 2023,39(3):181-226.
- [14] Yan L, Liu Y, Li WH, et al. Long-term outcomes of ultrasound-

- guided thermal ablation for the treatment of solitary low-risk papillary thyroid microcarcinoma; a multicenter retrospective study [J]. *Ann Surg*, 2023.
- [15] Cao XJ, Wang SR, Che Y, et al. Efficacy and safety of thermal ablation for treatment of solitary T1N0M0 papillary thyroid carcinoma; a multicenter retrospective study [J]. *Radiology*, 2021, 300(1): 209-216.
- [16] Geboers B, Scheffer HJ, Graybill PM, et al. High-voltage electrical pulses in oncology: irreversible electroporation, electrochemotherapy, gene electrotransfer, electrofusion, and electroimmunotherapy [J]. *Radiology*, 2020, 295(2): 254-272.
- [17] Xu D, Ge MH, Xu HX, et al. Expert consensus workshop report; guidelines for thermal ablation of thyroid tumors (2019 edition) [J]. *J Can Res Ther*, 2020, 16(5): 960.
- [18] Kim JH, Baek JH, Lim HK, et al. 2017 thyroid radiofrequency ablation guideline; Korean society of thyroid radiology [J]. *Korean J Radiol*, 2018, 19(4): 632-655.
- [19] Hu QL, Kuo JH. Choice in ablative therapies for thyroid nodules [J]. *J Endocr Soc*, 2023, 7(7): 78.
- [20] Yan L, Zhang MB, Song Q, et al. Ultrasound-guided radiofrequency ablation versus thyroid lobectomy for low-risk papillary thyroid microcarcinoma; a propensity-matched cohort study of 884 patients [J]. *Thyroid*, 2021, 31(11): 1662-1672.
- [21] van Dijk SPJ, Coerts HI, Gunput STG, et al. Assessment of radiofrequency ablation for papillary microcarcinoma of the thyroid; a systematic review and meta-analysis [J]. *JAMA Otolaryngol Head Neck Surg*, 2022, 148(4): 317-325.
- [22] Yan L, Li YY, Li X, et al. Clinical outcomes of ultrasound-guided radiofrequency ablation for solitary T1N0M0 papillary thyroid carcinoma; a retrospective study with more than 5 years of follow-up [J]. *Cancer*, 2023, 129: 2469-2478.
- [23] Li XY, Li J, Qiao Z, et al. Rigorous radiofrequency ablation can completely treat low-risk small papillary thyroid carcinoma without affecting subsequent surgical management [J]. *Eur Radiol*, 2022, 33: 4189-4197.
- [24] Scappaticcio L, Bellastella G. Dynamic risk stratification system provides a new paradigm to properly manage low-risk papillary thyroid microcarcinoma treated with radiofrequency ablation [J]. *Eur Radiol*, 2023; 1-3.
- [25] Yan L, Li XY, Li YY, et al. Comparison of ultrasound-guided radiofrequency ablation versus thyroid lobectomy for T1bN0M0 papillary thyroid carcinoma [J]. *Eur Radiol*, 2023, 33(1): 730-740.
- [26] Xiao J, Zhang Y, Yan L, et al. Ultrasonography-guided radiofrequency ablation for solitary T1aN0M0 and T1bN0M0 papillary thyroid carcinoma; a retrospective comparative study [J]. *Eur J Endocrinol*, 2021, 186(1): 105-113.
- [27] Tang WQ, Tang XY, Jiang DN, et al. Safety and efficacy of thermal ablation for cervical metastatic lymph nodes in papillary thyroid carcinoma; a systematic review and meta-analysis [J]. *Front Endocrinol (Lausanne)*, 2022, 13: 967044.
- [28] Song Q, Gao HJ, Ren L, et al. Radiofrequency ablation versus total thyroidectomy in patients with papillary thyroid microcarcinoma located in the isthmus; a retrospective cohort study [J]. *Int J Hypertherm*, 2021, 38(1): 708-714.
- [29] Zeng FQ, Zou B, Chen HB, et al. Analysis of therapeutic effect and influencing factors of ultrasound-guided radiofrequency ablation in the treatment of papillary thyroid microcarcinoma [J]. *J Ultrasound Med*, 2023, 42(8): 1769-1777.
- [30] Yan L, Zhang MB, Song Q, et al. Clinical outcomes of radiofrequency ablation for multifocal papillary thyroid microcarcinoma versus unifocal papillary thyroid microcarcinoma; a propensity-matched cohort study [J]. *Eur Radiol*, 2022, 32(2): 1216-1226.
- [31] Tufano RP, Pace-Asciak P, Russell JO, et al. Update of radiofrequency ablation for treating benign and malignant thyroid nodules. the future is now [J]. *Front Endocrinol*, 2021, 12: 698689.
- [32] Tuttle RM, Li D, Ridouani F. Percutaneous ablation of low-risk papillary thyroid cancer [J]. *Endocr Relat Cancer*, 2023, 30(3): e220244.
- [33] Lubner MG, Brace CL, Hinshaw JL, et al. Microwave tumor ablation; mechanism of action, clinical results, and devices [J]. *J Vasc Interv Radiol*, 2010, 21(8 Suppl): S192-S203.
- [34] Brace CL, Laeseke PF, Sampson LA, et al. Microwave ablation with multiple simultaneously powered small-gauge triaxial antennas; results from an *in vivo* swine liver model [J]. *Radiology*, 2007, 244(1): 151-156.
- [35] Tremblay BS, Douple EB, Ryan TP, et al. Effect of phase modulation on the temperature distribution of a microwave hyperthermia antenna array *in vivo* [J]. *Int J Hypertherm*, 1994, 10(5): 691-705.
- [36] Teng DK, Li WH, Du JR, et al. Effects of microwave ablation on papillary thyroid microcarcinoma; a five-year follow-up report [J]. *Thyroid*, 2020, 30(12): 1752-1758.
- [37] Wei Y, Niu WQ, Zhao ZL, et al. Microwave ablation versus surgical resection for solitary T1N0M0 papillary thyroid carcinoma [J]. *Radiology*, 2022, 304(3): 704-713.
- [38] Feng J, Jiang YZ, Feng YZ. Latest evidence of microwave ablation for papillary thyroid microcarcinoma compared with surgery; a systematic review and meta-analysis [J]. *Front Oncol*, 2023, 13: 1088265.
- [39] Lu C, Li XJ, Chu X, et al. Clinical effects of microwave ablation in the treatment of low-risk papillary thyroid microcarcinomas and related histopathological changes [J]. *Front Endocrinol (Lausanne)*, 2021, 12: 751213.
- [40] Ding M, Wu GS, Gu JH, et al. Pathology confirmation of the efficacy and safety of microwave ablation in papillary thyroid carcinoma [J]. *Front Endocrinol (Lausanne)*, 2022, 13: 929651.
- [41] 祖圆, 孙广永, 钱林学. 超声引导下微波消融治疗甲状腺微小乳头状癌后患者基因表达变化 [J]. *中国介入影像与治疗学*, 2023, 20(5): 282-285.
- Zu Y, Sun GY, Qian LX. Changes of gene expression in patients after ultrasound-guided microwave ablation of papillary thyroid microcarcinoma [J]. *Chin J Interv Imaging Ther*, 2023, 20(5): 282-285.
- [42] Zhou HD, Yu XY, Wei Y, et al. A clinical study on microwave ablation of multifocal (≤ 3) T1N0M0 papillary thyroid carcinoma [J].

- Eur Radiol, 2023, 33(6): 4034-4041.
- [43] Dong P, Teng DK, Sui GQ, et al. Long-term efficacy of microwave ablation for multifocal papillary thyroid microcarcinoma: a 5-year follow-up study[J]. Eur Radiol, 2023; 1-9.
- [44] Zhao ZL, Dong G, Wang SR, et al. Efficacy and safety of microwave ablation for the treatment of multifocal versus unifocal T1N0M0 papillary thyroid carcinoma: a propensity-matched multicentre retrospective study[J]. Eur Radiol, 2023.
- [45] Zheng L, Dou JP, Han ZY, et al. Microwave ablation for papillary thyroid microcarcinoma with and without US-detected capsule invasion: a multicenter prospective cohort study[J]. Radiology, 2023, 307(3): e220661.
- [46] 伍洁,魏莹,赵朕龙,等.超声引导下微波消融治疗侵犯被膜的甲状腺乳头状癌[J].中国介入影像与治疗学,2023,20(2):70-73. Wu J, Wei Y, Zhao ZL, et al. Ultrasound-guided microwave ablation for papillary thyroid carcinoma invading the capsule[J]. Chin J Interv Imaging Ther, 2023, 20(2): 70-73.
- [47] 吴冬倩,魏莹,赵朕龙,等.超声引导下微波消融治疗邻近被膜的甲状腺微小乳头状癌[J].中国介入影像与治疗学,2023,20(2):78-81. Wu DQ, Wei Y, Zhao ZL, et al. Ultrasound-guided microwave ablation for papillary thyroid carcinoma adjacent to the capsule[J]. Chin J Interv Imaging Ther, 2023, 20(2): 78-81.
- [48] 祁怡,李尊,倪静,等.超声引导下微波消融治疗甲状腺峡部乳头状癌[J].中国介入影像与治疗学,2023,20(2):82-85. Qi Y, Li Z, Ni J, et al. Ultrasound-guided microwave ablation for papillary thyroid carcinoma in isthmus[J]. Chin J Interv Imaging Ther, 2023, 20(2): 82-85.
- [49] Pacella CM, Bizzarri G, Guglielmi R, et al. Thyroid tissue: us-guided percutaneous interstitial laser ablation; a feasibility study[J]. Radiology, 2000, 217(3): 673-677.
- [50] 郭乐杭,徐辉雄.超声引导激光消融治疗甲状腺结节的进展[J].中华医学超声杂志(电子版),2013,10(5):360-363. Guo LH, Xu HX. Progress in ultrasound-guided laser ablation for thyroid nodules[J]. Chin J Med Ultrasound Electron Ed, 2013, 10(5): 360-363.
- [51] Zhang L, Zhou W, Zhou JQ, et al. 2022 Expert consensus on the use of laser ablation for papillary thyroid microcarcinoma[J]. Int J Hyperth, 2022, 39(1): 1254-1263.
- [52] Kim HJ, Chung SM, Kim H, et al. Long-term efficacy of ultrasound-guided laser ablation for papillary thyroid microcarcinoma: results of a 10-year retrospective study[J]. Thyroid, 2021, 31(11): 1723-1729.
- [53] Zhou W, Ni XF, Xu SY, et al. Ultrasound-guided laser ablation versus surgery for solitary papillary thyroid microcarcinoma: a retrospective study[J]. Int J Hyperth, 2019, 36(1): 896-903.
- [54] Valcavi R, Piana S, Bortolan GS, et al. Ultrasound-guided percutaneous laser ablation of papillary thyroid microcarcinoma: a feasibility study on three cases with pathological and immunohistochemical evaluation[J]. Thyroid, 2013, 23(12): 1578-1582.
- [55] Juan Z, Yongping L, Han XX, et al. A 5-year follow-up study on the efficacy and safety of ultrasound-guided laser ablation in elderly patients with papillary thyroid microcarcinoma: a retrospective, single-center study from China[J]. Front Endocrinol (Lausanne), 2022, 13: 972589.
- [56] Offi C, Misso C, Antonelli G, et al. Laser ablation treatment of recurrent lymph node metastases from papillary thyroid carcinoma[J]. J Clin Med, 2021, 10(22): 5295.
- [57] Spartalis E, Karagiannis SP, Plakopitis N, et al. Percutaneous laser ablation of cervical metastatic lymph nodes in papillary thyroid carcinoma: clinical efficacy and anatomical considerations[J]. Expert Rev Med Devices, 2021, 18(1): 75-82.
- [58] Ji LL, Wu Q, Gu J, et al. Ultrasound-guided percutaneous laser ablation for papillary thyroid microcarcinoma: a retrospective analysis of 37 patients[J]. Cancer Imaging, 2019, 19(1): 1-8.
- [59] Gao XM, Yang Y, Wang YT, et al. Efficacy and safety of ultrasound-guided radiofrequency, microwave and laser ablation for the treatment of T1N0M0 papillary thyroid carcinoma on a large scale: a systematic review and meta-analysis[J]. Int J Hyperth, 2023, 40(1): 2244713.
- [60] Tong MY, Li S, Li YL, et al. Efficacy and safety of radiofrequency, microwave and laser ablation for treating papillary thyroid microcarcinoma: a systematic review and meta-analysis[J]. Int J Hyperthermia, 2019, 36(1): 1278-1286.
- [61] Tasu JP, Tougeron D, Rols MP. Irreversible electroporation and electrochemotherapy in oncology: state of the art[J]. Diagn Interv Imaging, 2022, 103(11): 499-509.
- [62] Lyu Y, Zhang Y, Huang J, et al. A study on nonthermal irreversible electroporation of the Thyroid [J]. Technol Cancer Res Treat, 2019, 18: 1533033819876307.
- [63] Campana LG, Daud A, Lancellotti F, et al. Pulsed electric fields in oncology: a snapshot of current clinical practices and research directions from the 4th world congress of electroporation[J]. Cancers, 2023, 15(13): 3340.
- [64] 刘春苹,叶萍,张明悦.不可逆电穿孔对肿瘤消融的研究进展[J].介入放射学杂志,2023,32(5):498-502. Liu CP, Ye P, Zhang MY. Research progress in irreversible electroporation ablation for tumors[J]. J Interv Radiol, 2023, 32(5): 498-502.
- [65] Blazeviski A, Scheltema M, Amin A, et al. Irreversible electroporation (IRE): a narrative review of the development of IRE from the laboratory to a prostate cancer treatment [J]. BJU Int, 2020, 125(3): 369-78.
- [66] Bhutiani N, Philips P, Scoggins CR, et al. Evaluation of tolerability and efficacy of irreversible electroporation (IRE) in treatment of Child-Pugh B (7/8) hepatocellular carcinoma (HCC)[J]. HPB, 2016, 18(7): 593-599.
- [67] Gajewska-Naryniecka A, Szwedowicz U, Łapińska Z, et al. Irreversible electroporation in pancreatic cancer: an evolving experimental and clinical method[J]. Int J Mol Sci, 2023, 24(5): 4381.