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影像引导下前列腺定向穿刺活检术的研究进展*

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摘要: 确诊前列腺癌的金标准无疑是病理组织学检查,影像引导下的前列腺定向穿刺活检又是这当中最有效、最便捷的方式。而基于前列腺特异抗原(prostate specific antigen,PSA)筛查以及6分活检结果的前列腺癌诊断,已经由于其对低度肿瘤的过度诊断和对临床上有意义前列腺癌(格林森评分 ≥ 7)的诊断不足遭到批评。所以纵观国内外,影像引导已经增加到先用多参数MRI(multi-parametric magnetic resonance imaging,mpMRI)扫描检出病变组织再进行前列腺定向穿刺活检,包括in-bore MRI引导,认知融合引导,以及MRI/TRUS融合引导下的活检。本文就一些影像引导下前列腺定向穿刺活检术的研究进展进行综述。

关键词: 前列腺癌;穿刺活检;定向;MRI/TRUS

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Advances in Image-guided Targeted Prostate Biopsy*

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ABSTRACT: Undoubtedly, pathological findings is the golden standard for diagnosing prostate cancer. As we all know, targeted prostate biopsy under the guidance of image-guiding is the most efficient and the most convenient. Nevertheless, based on prostate specific antigen(PSA) screening and sextant biopsy, has been criticized for both overdiagnosis of low-grade tumors and underdiagnosis of clinically significant prostate cancers (Gleason score ≥ 7). So on viewing vertically of both national and abroad, image guidance has been added to perform targeted biopsies of lesions detected on multi-parametric magnetic resonance imaging (mpMRI) scans, including in-bore MRI-guided, cognitive fusion, and MRI/transrectal ultrasound fusion-guided biopsy. This review will examine advances in these image-guided targeted prostate biopsy techniques.

Key words: Prostate cancer; Biopsy; Targeted; MRI/TRUS

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前言

近年随着我国人口加速老龄化、生活方式西化等问题出现,前列腺癌已成为男性常见疾病,尤其在发达地区发病率迅速升高,如09年香港地区发病率就已经高出农村地区(2.17/10万)近10倍^[1]。为了获得早期治疗、延长生存年限,早期确诊前列腺癌成为首要步骤。虽然前列腺特异抗原(prostate specific antigen,PSA)异常增高对于提示前列腺癌敏感性很高^[2-4],但是它在前列腺增生、前列腺炎以及前列腺癌中特异性较差^[5],作为生物筛查标记不似从前受欢迎^[6-7]。所以,目前临床上诊断前列腺癌的金标准是穿刺活检的病理结果。然而,我们最常用的随机系统6分活检由于其敏感性、特异性都未达到理想状态,导致漏诊了部分临床上有意义的前列腺癌,并增加了对惰性癌的过度诊断。故我们应该开展利用MRI等更先进的影像技术来对前列腺进行定向穿刺活检,比如in-bore MRI引导,认知融合引导,以及MRI/TRUS融合引导下的活检。在这篇综述里我们将阐述探究这些不同的前列腺穿刺活检方法。

1 前列腺活检

1.1 TRUS 引导随机系统 6 分活检

临床上一旦血清PSA检查提示异常增高,就继以经直肠超声(Transrectal ultrasound,TRUS)行前列腺穿刺活检确诊。当前的穿刺标准是随机系统12-芯6分活检(systematic 12-core sextant biopsies,SBx),而非前列腺定向穿刺活检。最早前列腺穿刺活检是在触诊时以手指为引导进行的。20世纪80年代出现TRUS后,TRUS引导随机系统6分活检正式得以应用,与以手指为引导行结节活检相比,其显著增加了前列腺癌的检出^[8]。6分活检方法是获取前列腺左右两边的顶点、中点及低点的活检样本。随着1芯活检到2芯活检(中间的到侧面的),6分活检方案被扩大到每次SBx行12芯活检。这项技术使得前列腺癌的检出率从46%直接上升到了96%^[9,10],这种“扩大的抽样技术”也因此成为新的标准穿刺方案,但同时它却检出了更多的前列腺惰性癌^[11],并仍然漏诊了临床上三分之一的有意义前列腺癌^[12]。更重要的是,在大前列腺取样处较低时,尤其在不易进针的区域比如前列腺前侧,这项技术明显受到限制^[13]。另外在TRUS方面,由于超声图像上部分前列腺恶性肿瘤与正常组织间差别不明显,所以它更多用于前列腺不同区域的多处取

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样,从而也会导致探查更多的惰性癌以及漏掉在活检取样区域外的大肿瘤。如此,穿刺活检就会对 PSA 的筛查给予一个否定反馈。PSA 如果继续升高,患者就需再次行穿刺活检,遭受不必要的二次创伤;并且若多次穿刺活检结果仍为阴性,不但未能确诊,同时还会增加患者患脓毒症的风险^[14]。有证据直接表明 SBx 会漏掉 10-30% 的前列腺癌^[9],并且超过两次 SBx 检查的患者中超过 20% 的人会被诊断为前列腺癌^[15]。因此,尽管 SBx 方便、简单,但仅仅用它会漏掉部分有意义前列腺癌并造成对惰性癌的过度诊断。

1.2 In-bore MRI 引导活检

一个提高检出前列腺癌的有效方案是利用影像模型来进行前列腺定向穿刺活检,多参数 MRI (multi-parametric magnetic resonance imaging, mpMRI) 已经被证明在检测临床上有意义前列腺癌方面有很高的阳性和阴性预测值^[16]。其中,In-bore MRI 引导下的前列腺穿刺活检术在 21 世纪也已被若干团队验证^[17,18]。这项技术是在活检前利用有诊断价值的 mpMRI 获得病变组织位置,再经 MRI 引导取样。即患者取俯卧位,有诊断价值的 MRI 序列先定位到病变组织,接着将活检针直接在 MR 扫描架上通过经直肠或者经会阴的方式插入前列腺组织,并需再次证实活检针确是插入到已定位病变组织后再取样^[19]。这种方法的主要优势是病变样本精确化。比如,Hoeks 等^[20]对 PSA 升高并经 TRUS 引导下 SBx 穿刺阴性史的 265 名患者进行 in-bore MRI 引导下穿刺活检,其中 41% 的患者被检出前列腺癌,而且检出的大多数癌(87%)在临床上有意义。

然而,直接在 in-bore MRI 引导下的活检仍有相当大的限制,比如体位带来的不适,长时间操作(有报道称最短的操作时间是 19 分钟)带来的成本增加,以及对无磁性设备、无磁性穿刺针的需求^[21,22]。更重要的是,由放射科医生操作的这种方式泌尿外科医生并非会完全认可,所以这项技术在临床上未被广泛采纳^[23]。

1.3 认知融合引导活检

认知融合是极其简便的一种方法,除了 TRUS 器械以及 MRI 设备,不再需要其它任何附加设备。认知融合需要医生首先回顾分析前列腺的 MRI 图像,再利用 MRI 上的相关信息指导在 TRUS 下行前列腺定向活检。所以,这非常依赖操作者的经验以及其在没有充分物理知识储备的情况下将 MRI 结果转换成 TRUS 图像的能力。而且,相比超声常常用一系列的斜切面,MRI 却是用轴平面,这就导致在图像上它们是相交的,所以会增加更多的复杂性。最后,认知融合还不能追踪记录活检靶点与 US 上预定义靶点间的相关性。

在 2011 年,Haffner 和其同事^[24]评估了一组前列腺癌筛查指标异常(直肠指诊结果异常或者 PSA 升高)的 555 名患者。每名患者先进行前列腺 MRI 成像再进行 TRUS 引导下的定向 10-12 针系统活检(SBx),再另加在 MRI 上可疑区域的两针定向活检。对比发现,认知融合活检比 SBx 更能提高有意义癌的检出率($P<0.001$),其检出了 16% 的更高评分(格林森评分为 4 和 5)的肿瘤,更准确地评估了肿瘤负荷($P=0.002$)。Sciarra 等^[25]在研究中将穿刺阴性史的患者和 PSA 升高的患者随机分配到 TRUS 引导的系统活检或认知融合引导下的定向活检。结果

也表明认知融合活检组检出有意义前列腺癌的准确率很高,高达 90.7%,并且认知融合活检组前列腺癌的诊断率几乎是 TRUS 组的两倍(46% vs 24%)。此外,Park 等^[26]进行了一个相似的前瞻性研究,研究对象是无穿刺史的 PSA 升高的患者。再一次证明,认知融合活检有更高的检出率(29.5% vs 9.8%, $P=0.03$)和更高的有意义阳性检出率(9.9% vs 2.5%, $P=0.002$)。

在另一个研究中,Labanaris 和其同事^[27]将穿刺阴性史的 260 名患者进行 mpMRI 成像,如果患者 MRI 阴性则进行 18-芯 TRUS 活检,如果患者 MRI 提示可疑癌则进行 18-芯 TRUS+ 认知融合活检。这项研究发现在 MRI 上就有 65% 的患者提示可疑癌,认知融合活检对有意义前列腺癌的检出率明显更高(56% vs 18%)。并且,Park 等^[26]那项研究还对 95 名有局限性前列腺癌的患者进行了定向 MRI/TRUS 融合活检和 TRUS 引导的 SBx 方案的对比分析。患者先进行 4-芯定向活检,再进行 12-芯 SBx。结果表明相对于系统活检,定向活检能更好地检出癌症部分($P=0.003$)。尽管这项研究仍被 MRI 引导下的的大数量活检偏差影响,但其消除了 Lebanaris' 研究的偏差。

以上多项证据表明,相比于 TRUS 引导的随机系统活检,认知融合活检对前列腺癌靶点更为精确。然而,由于认知融合技术对操作者的强烈依赖性,即训练操作者达到一致性、可复性方面的限制,导致在临床上也未能被广泛应用^[24,26,27]。

1.4 MRI/TRUS 融合引导活检

MRI/TRUS 融合技术的主要概念是利用软件联合记录 MRI 和实时超声两种影像的优势,再用于前列腺定向活检。mpMRI 提供确切的肿瘤位置、大小的信息,TRUS 为活检提供实时引导。因此,这项技术首先进行 MRI 扫描,在扫描中将前列腺边界和肿瘤位置进行分段,并将这些信息通过电子发送到活检套件上。然后行三维超声成像,在超声扫描中再分段,并通过记录软件将其与前列腺的 MRI 图像进行融合,最后再进行定向活检。同时在过程中通过严格手写或用软件来记录两种显像方式的弹性信息,以此帮助消除一些瞄准前列腺癌靶点的“认知融合”偏差。而这种弹性匹配在很大程度上取决于高质量的超声扫描,所以为避免不重合或不正确的扭曲记录,我们必须对前列腺顶点-低点进行正确的超声扫描。超声和 MRI 间的合作还需考虑到对 TRUS 穿刺针实时情况的处理以及在 MRI 上对相应切面旋转和变换的观察。

这项技术在欧美国家得到广泛应用,国外有若干研究^[28-31]表明 MRI/TRUS 融合引导活检能大大检出 SBx 方案漏掉的前列腺癌,同时也有研究^[32]表明,MRI/TRUS 融合引导下的前列腺定向活检能极大提高临床上有意义前列腺癌的检出率,但在我国,目前尚无应用 MRI/TRUS 融合穿刺活检术的报道。

2 总结

目前 TRUS 引导随机系统活检仍然是诊断前列腺的标准方案,但我们也应该越来越认识到它的局限性。为了提高临床上有意义前列腺癌的检出率,同时减少对惰性癌的过度诊断,我们应该开展利用 MRI 等更先进的影像技术来对前列腺进行定向活检。并且,由于近来 MRI 大容量的优势以及靶向技术检出有意义病变的优势,将来可能会需要更少的活检针数,这就会大大减少活检后脓毒症的发生。当然,图像融合引导下的前

表 1 TRUS 引导, in-bore MRI 引导, 认知融合引导, 以及 MRI/TRUS 融合引导前列腺活检术间的对比

Table 1 Comparison of TRUS-guided, in-bore MRI-guided, cognitive fusion, and MRI/TRUS fusion prostate biopsy techniques

Prostate Biopsy Comparison	Random systematic TRUS-guided	in-bore MRI-guided	Cognitive Fusion	MRI/TRUS Fusion
Real-time targeting	×	×	√	√
Spatial resolution	×	√	×	√
Cost-effectiveness	√	×	√	√
Location record	×	√	×	√
Use by urologist	√	×	√	√
Time-consuming	×	√	×	×

列腺活检技术要作为新的治疗方案被临床广泛采纳应用, 最终也是需要接受大规模, 多参数, 随机研究结果的验证。

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(上接第 797 页)

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