聚乳酸–羟基乙酸共聚物微球瘤内注射抑制荷人三阴性乳腺癌裸鼠移植瘤细胞的增殖*★

柯丽明，张秀娟，何以敕，林礼务，薛恩生，陈志奎

Inhibitory effect of poly (lactic-co-glycolic acid) microspheres containing docetaxel intratumoral injection on the proliferation of human triple negative breast cancer xenograft in nude mice

Ke Li-ming, Zhang Xiu-juan, He Yi-mi, Lin Li-wu, Xue En-sheng, Chen Zhi-kui

文章亮点：

超声引导下瘤内注射多西他赛聚乳酸–羟基乙酸微球可明显抑制荷人三阴性乳腺癌裸鼠移植瘤增殖，高效、安全且操作方便。

Department of Ultrasound, Union Hospital, Fujian Medical University, Fuzhou 350001, Fujian Province, China

Ke Li-ming★, Studying for master's degree, Physician, Department of Ultrasound, Union Hospital, Fujian Medical University, Fuzhou 350001, Fujian Province, China
woshikeliming@163.com

Corresponding author: Chen Zhi-kui, Doctor, Associate chief physician, Department of Ultrasound, Union Hospital, Fujian Medical University, Fuzhou 350001, Fujian Province, China
jimchen2003@163.com

Supported by: Young Core Instructor Foundation of Fujian Medical University, No. [2010]7*

doi:10.3969/j.issn.2095-4344.2012.29.018

Received: 2012-01-24
Accepted: 2012-04-05

Abstract

BACKGROUND: Under ultrasound guidance, intratumoral injection of sustained-released chemotherapeutics for tumor interstitial chemotherapy can improve antitumor and decrease systemic toxicity and side effects.

OBJECTIVE: To investigate the inhibitory effect of poly (lactic-co-glycolic acid) (PLGA) microspheres containing docetaxel intratumoral injection under ultrasound guidance on the proliferation of human triple negative breast cancer xenograft.

METHODS: Sustained-release PLGA microspheres containing docetaxel was prepared by solvent evaporation method. The morphology and particle size were observed by scanning electron microscope. The drug loading rate, entrapment efficiency and *in vitro* release were examined by high performance liquid chromatography. The human triple negative breast cancer-bearing nude mouse model was established and divided into five groups: model group (with no treatment), microspheres group (injected blank PLGA microspheres), docetaxel intratumoral injection group (injected 10 mg/kg docetaxel and administrated once every 10 days for 40 days continuously), PLGA microspheres containing docetaxel low-dose group (injected drug-released microspheres intratumorally: 20 mg/kg docetaxel one time) and PLGA microspheres containing docetaxel high-dose group (injected 40 mg/kg docetaxel one time)

RESULTS AND CONCLUSION: The mean particle size of prepared PLGA microspheres containing docetaxel was detected as 23.1 μm with an optimal entrapment efficiency of 96.3%, drug loading rate of 4.82%, and cumulative release drug rate of 85.7% within 40 days. Under ultrasound guidance, intratumoral injection of PLGA microspheres containing docetaxel displayed a potent antitumor effect on human triple negative breast cancer xenograft. And the tumor inhibition rate of the high-dose group had reached 65.7%. Color Doppler ultrasound showed the tumor blood supply was significantly decreased. Pathological examination indicated that the tumor tissues were found a great of putrescence. These findings suggest that interstitial chemotherapy by using ultrasound-guided intratumoral injection of PLGA microspheres containing docetaxel can significantly inhibit the proliferation of human triple negative breast cancer xenograft.

Ke LM, Zhang XJ, He YM, Lin LW, Xue ES, Chen ZK. Inhibitory effect of poly (lactic-co-glycolic acid) microspheres containing docetaxel intratumoral injection on the proliferation of human triple negative breast cancer xenograft in nude mice. Zhongguo Zuzhi Gongcheng Yanjiu. 2012;16(29): 5407-5411. [http://www.crter.cn http://en.zglckf.com]

摘要

背景：通过超声引导，将抗肿瘤药物缓释剂注射到肿瘤局部进行间质化疗，可提高抗肿瘤效果，并且减轻全身毒副作用。

目的：观察超声引导下瘤内注射多西他赛聚乳酸–羟基乙酸微球对荷人三阴性乳腺癌裸鼠移植瘤增殖的抑制作用。

方法：采用乳化溶剂挥发法制备多西他赛聚乳酸–羟基乙酸微球，扫描电镜观察微球的表面形态及粒径，高效液相色谱法测定包封率、载药率及体外释放情况。建立荷人三阴性乳腺癌裸鼠移植瘤模型，随机分为5组：模型组无处理；微球组在肿瘤内注射空白聚乳酸–羟基乙酸微球1次；多西他赛瘤内注射组在肿瘤内注射多西他赛注射液(多西他赛剂量为10 mg/kg)，每10 d给药1次，连续4次；多西他赛聚乳酸–羟基乙酸共聚物微球低剂量组在肿瘤内注射载药微球(多西他赛剂量为20 mg/kg)1次；多西他赛聚乳酸–羟基乙酸共聚物微球高剂量组在肿瘤内注射载药微球(多西他赛剂量为40 mg/kg)1次。

结果与结论：多西他赛聚乳酸–羟基乙酸微球平均粒径23.1 μm，包封率为96.3%，载药率为4.82%，40 d累积释放药物85.7%。超声引导下多西他赛聚乳酸–羟基乙酸微球瘤体内注射具有明显的抗肿瘤作用，高剂量组抑瘤率达65.7%，彩色多普勒超声见肿瘤血流信号明显减少，病理学检查见肿瘤组织大片坏死，提示超声引导下瘤内注射多西他赛聚乳酸–羟基乙酸微球可明显抑制荷人三阴性乳腺癌裸鼠移植瘤增殖。

福建医科大学附属协和医院超声科，福建省福州市 350001

柯丽明★，女，1985 年生，福建省莆田市人，福建医科大学在读硕士，医师，主要从事乳腺癌超声诊断与介入治疗的研究。
woshikeliming@163.com

通讯作者：陈志奎，博士，副主任医师，福建医科大学附属协和医院超声科暨福建省超声医学研究所，福建省福州市 350001
jimchen2003@163.com

中图分类号:R318
文献标识码:B
文章编号:2095-4344(2012)29-05407-05

收稿日期: 2011-10-24
修回日期: 2012-04-05
(20111024012/W · T)

关键词：乳酸-羟基乙酸；超声；微球；多西他赛；乳腺癌；生物材料

缩略语：聚乳酸-羟基乙酸共聚物(poly(lactic-co-glycolic acid)，PLGA)；多西他赛 PLGA 微球(PLGA microspheres containing docetaxel，PMCD)

柯丽明，张秀娟，何以敉，林礼务，薛恩生，陈志奎. 聚乳酸-羟基乙酸共聚物微球瘤内注射抑制荷人三阴性乳腺癌裸鼠移植瘤细胞的增殖[J].中国组织工程研究，2012，16(29):5407-5411.
[http://www.crter.org http://cn.zglckf.com]

0 引言

目前临床上使用的化疗药物大多缺乏肿瘤细胞特异性，全身给药常导致各种毒副作用，如心脏、肝脏、肾脏、神经系统等毒性。通过超声引导，将化疗药物缓释制剂注射到肿瘤局部进行间质化疗，可维持肿瘤局部较高的药物浓度，并且明显减轻机体的毒副作用[1-2]。本实验旨在探讨超声引导多西他赛聚乳酸-羟基乙酸共聚物(poly(lactic-co-glycolic acid)，PLGA)微球瘤内注射治疗三阴性乳腺癌的有效性和可行性，为乳腺癌治疗探索新的思路。

1 材料和方法

设计：观察性实验。

时间及地点：实验于2011-03/09在福建省超声医学研究所完成。

材料：

细胞系：人乳腺癌细胞MDA-MB-231由中国科学院上海细胞库提供。

实验动物：无特定病原体(SPF级)裸鼠BALB/c-nu/nu，雌性，体质量(15±1) g，由上海斯莱克实验动物有限公司提供，合格证号SCXK(沪)2007-0005。

主要原料及仪器：

原料及仪器	来源
多西他赛原料药	湖北宏中药业有限公司
聚乳酸羟基乙酸	山东医疗器械研究所
悬臂式机械搅拌器	德国 IKA 公司
高效液相色谱仪	日本岛津公司
彩色超声诊断仪	德国西门子公司

实验方法：

多西他赛 PLGA 微球(PLGA microspheres containing docetaxel，PMCD)的制备及性质测定：称取PLGA 1 000 mg，溶于5 mL二氯甲烷，加入50 mg多西他赛，溶解后注入50 mL 1%聚乙烯醇溶液中，600 r/min机械搅拌2 min，继续低速磁力搅拌4 h使微球固化，真空冷冻干燥即为PMCD[3]。取适量PMCD冻干粉，均匀涂布于双面胶带上，溅金后扫描电镜观察表面形态及粒径。精密称取10 mg PMCD，加入0.5 mL二氯甲烷溶解，再加入2.5 mL甲醇，取20 μL进样行高效液相色谱检测包封率和载药率。

包封率(%)=(载药微球实际载药量/理论载药量)×100%
载药率(%)=(载药微球多西他赛质量/载药微球质量)×100%

精密称取PMCD 5 mg，加入100 mL磷酸盐缓冲液(0.02 mol/L，pH 7.2，含 0.02% NaN_3)，37 ℃、(75±5) r/min振荡，分别于第1，10，20，30，40天取样，高效液相色谱检测多西他赛释放量。

荷人三阴性乳腺癌裸鼠移植瘤模型的建立：大量扩增人乳腺癌细胞 MDA-MB-231，2.5 g/L胰蛋白酶-EDTA消化，收集细胞，用生理盐水洗涤2次，调整细胞浓度为2×10^7 L^{-1}，每只裸鼠右前肢内侧乳头下接种0.1 mL细胞悬液。

动物分组与治疗：裸鼠接种乳腺癌细胞悬液14 d后，选取肿瘤最大径1.2~1.5 cm的裸鼠25只，随机分为5组，每组5只。乙醚吸入麻醉后，在超声引导下进行瘤内注射治疗，尽量使药物均匀分布于整个肿瘤。模型组：无处理；微球组：肿瘤内注射空白PLGA微球1次；多西他赛瘤内注射组：肿瘤内注射多西他赛注射液(多西他赛剂量为10 mg/kg)，每10 d给药1次，连续4次；PMCD低剂量组：肿瘤内注射载药微球(多西他赛剂量为20 mg/kg)1次；PMCD高剂量组：肿瘤内注射载药微球(多西他赛剂量为40 mg/kg)1次。

抗肿瘤疗效观察：给药后第40天，各组荷瘤裸鼠乙醚麻醉后进行彩色多普勒超声检查，观察肿瘤形态、内部回声、血流信号等。颈椎脱

臼处死裸鼠，剥离肿瘤称质量，根据公式计算肿瘤生长抑制率。

抑制率(%)=(1−治疗组平均瘤质量/模型组平均瘤质量)×100%

切取肿瘤组织，体积分数10%甲醛固定，常规石蜡包埋切片，苏木精-伊红染色，光学显微镜下观察肿瘤病理变化。

主要观察指标：①PMCD的粒径、包封率、载药率。②荷人乳腺癌裸鼠肿瘤的生长抑制率、彩色多普勒超声影像检查、病理组织学分析。

统计学分析：计量资料以$\bar{x}\pm s$表示，采用SPSS 16.0统计软件包进行t 检验，以$P < 0.05$为差异有显著性意义。

2 结果

2.1 实验动物数量分析 实验选用裸鼠25只，分为5组，无脱失，全部进入结果分析。

2.2 PMCD形态及体外释放曲线 制备的PMCD呈圆球形、表面光滑、分散良好，平均粒径为23.1 μm。高效液相色谱法测得包封率为96.3%，载药率为4.82%，PMCD在体外平稳释放，无明显突释效应，第1天释放了7.2%，至第40天累积释放了85.7%，见图1。

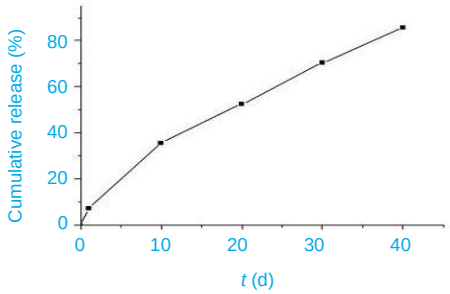

Figure 1 *In vitro* release curve of poly (lactic-co-glycolic acid) microspheres containing docetaxel
图 1 PMCD 体外释放曲线图

2.3 彩色多普勒超声观察 模型组裸鼠肿瘤形态尚规则，血流信号丰富，见图2，而载药微球组，尤其是高剂量组裸鼠肿瘤明显缩小，血流信号明显减少，仅于瘤体周边检测到少量血流信号，见图3。

2.4 肿瘤生长抑制率 PMCD高剂量组裸鼠肿瘤质量明显小于模型组，二者比较差异有非常显著性意义($P < 0.01$)，其肿瘤生长抑制率达65.7%，亦明显高于多西他赛组及PMCD低剂量组，见表1。

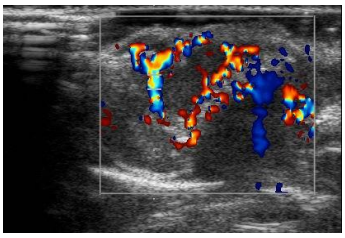

Figure 2 Color Doppler ultrasound results of the tumor from nude mice in the model group
图 2 模型组裸鼠肿瘤彩色多普勒超声表现

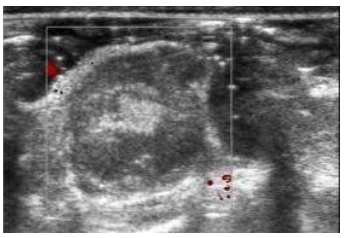

Figure 3 Color Doppler ultrasound results of the tumor in docetaxel microspheres high-dose group
图 3 多西他赛微球高剂量组肿瘤彩色多普勒超声表现

表 1 不同治疗组抑瘤率比较
Table 1 The comparison of tumor inhibition rate in different treatment groups

Group	Tumor weight ($x\pm s$, g)	IR (%)
Model	3.5±0.8	–
Blank microspheres	3.7±0.9	–
Docetaxel intratumoral injection	1.8±0.3[ab]	48.6
Low-dose	1.6±0.3[ab]	54.3
High-dose	1.2±0.2[a]	65.7

[a]$P < 0.01$, *vs.* model group; [b]$P < 0.05$, *vs.* high-dose group

2.5 病理组织学检查 模型组肿瘤组织光学显微镜观察见细胞核大染色深，病理性核分裂相增多，见图4，而PMCD高剂量组肿瘤组织大片变性坏死，部分组织结构模糊不清，见图5。

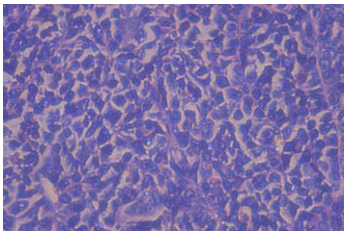

Figure 4 Pathological image of tumor tissues in nude mice of the model group (×400)
图 4 模型组裸鼠肿瘤组织病理表现(×400)

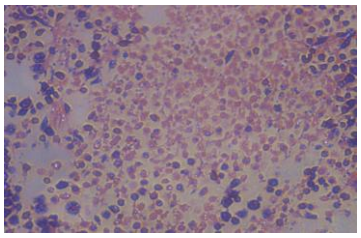

Figure 5 Pathological histology image of tumor in docetaxel microspheres high-dose group (×400)
图 5 多西他赛微球高剂量组肿瘤病理组织学表现(×400)

3 讨论

随着高分子材料在医药学领域的应用，微球、脂质体、凝胶、聚合物胶束等药物缓释新制剂成为研究热点[3-13]，这些缓释制剂不但提高了包裹药物的稳定性，维持药物稳定释放，降低药物的全身毒副作用，并且通过局部注射可达到肿瘤靶向治疗的效果[14-15]。PLGA是目前制备缓释微球和组织工程的常用材料，生物相容性好，并且可生物降解，最终分解成二氧化碳和水排出体外[16-17]。

本实验采用乳化溶剂挥发法制备的PMCD粒径23.1 μm[18]，包封率、载药率高。载药微球在超声观察下呈高至强回声，采用超声引导瘤内注射给药的方法，可实时观察进针路径及药物在肿瘤内分布是否均匀，必要时进行补充注射，确保整个肿瘤均可得到高浓度的药物，提高治疗精确性与有效性。PMCD具有良好的缓释效果，可持续释放药物达40 d，注射到肿瘤局部缓慢释放药物，可维持局部较高的药物浓度，并且明显减轻机体毒副作用，裸鼠瘤内一次性注射含40 mg多西他赛的微球，裸鼠一般情况良好，未见明显毒副作用。

乳腺癌是危害妇女健康的主要恶性肿瘤之一，其中三阴性乳腺癌占10%~20%[19-20]，其雌激素受体、孕激素受体和人表皮生长因子受体2表达均缺失，侵袭力强、远处转移风险高、预后较差[21-23]。由于缺乏相应受体不能进行内分泌及生物治疗，目前这种特殊类型乳腺癌的全身治疗仅限于化疗[24-25]。但全身化疗存在肿瘤局部药物浓度低，而毒副作用大等缺点[26]。高频彩色多普勒超声检查已经广泛应用于乳腺肿瘤的诊断与介入治疗[27-28]，在超声引导下，将化疗药物注射到乳腺癌局部进行间质化疗可明显减轻全身化疗的毒副反应。

多西他赛通过促进微管双聚体装配成微管，同时通过防止去多聚化过程而使微管稳定，阻滞细胞于G_2和M期，从而抑制癌细胞的有丝分裂和增殖[29-30]。本实验在超声引导下，将多西他赛微球注射到荷人三阴性乳腺癌裸鼠移植瘤内，显示出良好的抗肿瘤作用。高剂量组肿瘤体积增长明显受到抑制，其肿瘤生长抑制率达65.7%，明显高于多西他赛注射液瘤内注射，亦高于多西他赛微球低剂量组，具有一定的剂量依赖效应。彩色多普勒超声及病理组织学检查结果亦表明多西他赛微球组抗肿瘤作用明显优于多西他赛瘤内注射组，其原因主要是多西他赛微球在肿瘤内缓慢释放，维持肿瘤局部长时间、高浓度的药物量，从而提高了抗肿瘤效果，减轻毒副作用，显示出高效安全的优势。

综上所述，超声引导下多西他赛PLGA微球瘤内注射间质化疗可明显抑制荷人三阴性乳腺癌裸鼠移植瘤增殖，高效、安全且操作方便，具有潜在的临床应用价值。

4 参考文献

[1] Chen ZK, Lin LW, Yang YH, et al. US-guided interstitial chemotherapy using paclitaxel temperature-responsive gel for breast cancer treatment in rat. J Cancer Res Clin Oncol.2010; 136(4):537-545.
[2] Chen ZK,Lin LW,Yang YH,et al.Interstitial chemotherapy using thermosensitive gel-coated ricin in nude mice bearing a human hepatoma. Hepatol Res.2010;40(2):188-195.
[3] Tang G, Zhang H, Zhao Y, et al. Prolonged release from PLGA/HAp scaffolds containing drug-loaded PLGA/gelatin compositemicrospheres. J Mater Sci Mater Med.2012;23(2): 419-429.
[4] Ghassemi AH, van Steenbergen MJ, Barendregt A,et al. Controlled release of octreotide and assessment of peptide acylation from poly(D,L-lactide-co-hydroxymethyl glycolide) compared to PLGA microspheres. Pharm Res.2012;29(1): 110-120.
[5] Hirota K, Hasegawa T, Nakajima T,et al. Phagostimulatory effect of uptake of PLGA microspheres loaded with rifampicin on alveolar macrophages. Colloids Surf B Biointerfaces.2011; 87(2):293-298.
[6] Pohlen U, Buhr HJ, Berger G. Improvement of biodistribution with PEGylated liposomes containing docetaxel with degradable starch microspheres for hepatic arterial infusion in the treatment of liver metastases: a study in CC-531 liver tumor-bearing WAG RIJ rats. Anticancer Res.2011;31(1): 153-159.
[7] Yang FY, Teng MC, Lu M,et al. Treating glioblastoma multiforme with selective high-dose liposomal doxorubicin chemotherapy induced by repeated focused ultrasound. Int J Nanomedicine.2012;7:965-974.
[8] Paliwal SR, Paliwal R, Pal HC,et al. Estrogen-anchored pH-sensitive liposomes as nanomodule designed for site-specific delivery of doxorubicin in breast cancer therapy. Mol Pharm.2012;9(1):176-186.
[9] Zhang C, Ding Y, Yu LL, et al. Polymeric micelle systems of hydmxycamptothecin based on amphiphilic N-alkyl-Ntrimethyl chitosan derivatives. Colloids and Surfaces B:Biointerfaces. 2007;55(2):192.

[10] Fan L, Wu H, Zhang H, et al. Novel super PH-sensitive nanoparticles responsive to tumor extracellular PH. Carbohydrate Polymers. 2008;3(73):390.
[11] Harada A, Kataoka K. Supramolecular assemblies of block copolymers in aqueous media as nanocontainers relevant to biological applications. Progress in Polymer Science.2006; 31(11):949-982.
[12] Ren J,Hong HY,Ren TB,et al. Preparation and characterization of magnetic PLA-PEG composite particles. Materials Letters. 2005;59(21):2655-2658.
[13] Zhang JX,Qiu LY,Jin Y,et al. Controlled nanoparticles formation by self-assembly of novel amphiphilic polyphosphazenes with poly (N- isopropylacrylamide) and ethyl glycinate as side groups. Reactive & Functional Polymers.2006;66(12):1630-1640.
[14] Khan W，Kumar N. Drug targeting to macrophages using paromomycin- loaded albumin microspheres for treatment of visceral leishmaniasis: an in vitro evaluation. J Drug Target. 2011;19(4):239-250.
[15] Cho JK，Hong KY，Park JW, et al.Injectable delivery system of 2-methoxyestradiol for breast cancer therapy using biodegradable thermosensitive poly (organophosphazene) hydrogel. J Drug Target.2011;19(4):270-280.
[16] Toti US，Guru BR，Hali M, et al.Targeted delivery of antibiotics to intracellular chlamydial infections using PLGA nanoparticles. Biomaterials.2011;32(27):6606-6613.
[17] Lee ES，Park KH，Park IS，et al. Glycol chitosan as a stabilizer for protein encapsulated into poly(1actide-co-glycolide) microparticle. Int J Pharm.2007;338(1-2):310-316.
[18] Chen ZK, Cai MX, Yang J, et al. Chemotherapy with PLGA microspheres containing docetaxel decreases angiogenesis in human hepatoma xenograft. Med Oncol.2012;29(1):62-69.
[19] Rakha EA, El-Sayed ME, Gleen AR. Prognostic markers in triple-negative breast cancer. Cancer.2007;109(1):25-32.
[20] Carey LA, Perou CM, Livasy CA, et al. Race, breast cancer subtypes, and survival in the Carolina Breast Cancer Study. 2006;295(21):2492-2502.
[21] Kurebayashi J.Possible treatment strategies for triple-negative breast cancer on the basis of molecular characteristics.Breast Cancer.2009;16(4):275-280.
[22] Yamamoto Y,Iwase H.Clinicopathological features and treatment strategy for triple-negative breast cancer.IntJ Clin Oncol.2010;15(4):341-351.
[23] Dent R, Hanna WM, Trudeau M, et al. Pattern of metastatic spread in triple-negative breast cancer. Breast Cancer Res Treat.2009;115(2): 423-428.
[24] Dawson SJ, Provenzano E, Caldas C. Triple negative breast cancers: clinical and prognostic implications. Eur J Cancer. 2009;45(1):27-40.
[25] Wang YJ,Wang N,Wang B,et al.Zhonghua Zhongliu Zazhi. 2009; 31(5):346-350.
王雅杰,王宁,王斌,等.三阴性乳腺癌与人表皮生长因子受体2过表达乳腺癌患者的临床病理特征和预后分析[J].中华肿瘤杂志, 2009,31(5):346-350.
[26] Ten Tije AJ,Verweij J,Carducci MA, et al.Prospective Evaluation of the Pharmacokinetics and Toxicity Profile of Docetaxel in the Elderly. Clin. Oncol.2005;23(6):1070-1077.
[27] Wu XP,Song QH,Du YL.Zhongguo Yixue Yingxiang Jishu. 2011; 27(5):971-974.
吴秀平,宋庆华,杜毅力.二维超声多普勒超声及弹性成像鉴别诊断乳腺肿块[J].中国医学影像技术,2011,27(5):971-974.
[28] Shi J,Wang B,Liu YH. Zhongguo Yixue Yingxiang Jishu. 2010; 26(5):877-880.
石健,王彬,刘荫华. 乳腺高频彩色多普勒超声检查中应用BI-RADS分级诊断标准对乳腺疾病的诊断价值[J].中国医学影像技术,2010,26(5):877-880.
[29] Morse DL, Gray H, Payne CM, et al. Docetaxel induces cell death through mitotic catastrophe in human breast cancer cells. Mol Cancer Ther.2005;4(10):1495-1504.
[30] Montero A, Fossella F, Hortobagyi G, et al. Docetaxel for treatment of solid tumors:a systematic review of clinical data. Lancet Oncol.2005; 6(4):229-239.

来自本文课题的更多信息--

基金声明: 福建医科大学青年骨干教师基金(协院科[2010]7 号)。

作者贡献: 设计、实施、评估者分别为通讯作者与第一、二作者，无盲法评估。

利益冲突: 课题未涉及任何厂家及相关雇主或其他经济组织直接或间接的经济或利益的赞助。

伦理要求: 实验过程中对动物的处置应符合 2009 年《Ethical issues in animal experimentation》相关动物伦理学标准的条例。

文章概要:

文章要点: 制备载多西他赛的聚乳酸-羟基乙酸缓释微球，观察表面形态，测定载药微球的粒径、载药率、包封率、体外释放等，在超声引导下瘤内注射治疗荷人三阴性乳腺癌裸鼠移植瘤，评价其抗肿瘤作用。

关键信息: ①乳化溶剂挥发法制备的多西他赛 PLGA 微球粒径均匀、包封率高，缓释效果好。②超声引导下瘤体内注射多西他赛微球治疗荷人三阴性乳腺癌裸鼠移植瘤具有高效安全的特点。

研究的创新之处与不足: ①创新之处: 超声实时监测多西他赛微球瘤体内注射治疗乳腺癌，可保证整个肿瘤得到均匀的高浓度药物治疗，高效安全。②不足之处: 裸鼠个体小，难以进行原位肿瘤接种。