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Imaging features of radiofrequency ablation with heat deployed liposomal doxorubicin in hepatic tumors

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Abstract

Introduction—The imaging features of unresectable hepatic malignancies that underwent radiofrequency ablation (RFA) in combination with lyso-thermosensitive liposomal doxorubicin (LTLD) were determined.

Materials and Methods—A phase I dose escalation study combining RFA with LTLD was performed with peri- and post- procedural CT and MRI. Imaging features were analyzed and measured in terms of ablative zone size and surrounding penumbra size. The dynamic imaging appearance was described qualitatively immediately following the procedure and at one month follow-up. The control group receiving liver RFA without LTLD was compared to the study group in terms of imaging features and post ablative zone size dynamics at follow-up.

Results—Post treatment scans of hepatic lesions treated with RFA and LTLD have distinctive imaging characteristics when compared to those treated with RFA alone. The addition of LTLD

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Conflict of Interest Statement

National Institutes of Health and Celsion Corp have a cooperative research and development agreement. Dr. Riccardo Lencioni is a consultant for Celsion Corp.

Ethical Approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent

Informed consent was obtained from all individual participants included in the study

resulted in a regular or smooth enhancing rim on T1W MRI which often correlated with increased attenuation on CT. The LTLD treated ablation zones were stable or enlarged in the four weeks following ablation in 69% of study subjects as opposed to conventional RFA where the ablation zone underwent involution compared to immediate-post procedure.

Conclusion—The imaging features following RFA with LTLD were different from those after standard RFA and can mimic residual or recurrent tumor. Knowledge of the subtle findings between the two groups can help avoid misinterpretation and proper identification of treatment failure in this setting. Increased size of the LTLD treated ablation zone after RFA suggests ongoing drug-induced biological effects.

Introduction

Radiofrequency ablation (RFA) is a widely accepted treatment of choice for unresectable hepatic neoplasms and intrahepatic distant recurrences [1], but may be limited by the size of the lesion that can be treated. Currently, large lesions (>3 cm in diameter) suffer from higher or unacceptable failure rates [2–6]. Although surgical resection remains the gold standard for HCC [7–9], only approximately 20% of patients are candidates for this therapy [10]. Expanding the indications for local hepatic RFA could potentially result in more patients benefitting from this locoregional therapy with less untreated microscopic disease in the treatment margins [4].

The addition of heat deployed chemotherapy applied locally in the periphery of the thermal lesion could provide more effective therapy through concentrating the drug in the area of highest treatment failure. Low temperature sensitive liposomes that release doxorubicin at temperatures greater than 39.5°C have been developed (ThermoDox®, Celsion Corp, Columbia, MD). *In vitro* models using lyso-thermosensitive liposomal doxorubicin (LTLD) have shown that doxorubicin is deposited at the highest concentrations within 1cm outside the ablation zone [11]. The dual benefits of this approach consist of reducing systemic toxicity of the chemotherapeutic agent while exposing the tumor site, particularly the tumor or treatment margin, to a higher concentration gradient of the drug.

A Phase I clinical trial evaluated the safety of LTLD administration, in conjunction with RFA, in unresectable hepatic malignancies and determined the maximum tolerated dose (MTD) of the LTLD to be 50 mg/m² [12]. A recently completed randomized controlled phase III clinical trial used this LTLD and RFA in combination to treat HCC tumors 3-7 cm with high local failure rates from RFA. This trial was considered to be a Priority Clinical Trial for HCC at the National Cancer Institute's Clinical Trials Planning Meeting [13].

Post-treatment imaging from the Phase I clinical trial revealed characteristics unlike those of typical post-ablative lesions [14]. The CT features of hepatic lesions in the period following RFA enhanced by LTLD are described, as Response Evaluation Criteria in Solid Tumors and World Health Organization criteria do not apply to ablated lesions [15]. The purpose of this analysis is to characterize these atypical imaging findings which may assist radiologists in determining a more accurate assessment of treatment response after this dual therapy. As the future use of RFA and LTLD increases, diagnostic and interventional radiologists should

be familiar of the imaging features following this combined locoregional therapy in order to avoid misinterpretation of drug effects for residual or recurrent tumor.

Typical CT imaging features of RFA

On contrast-enhanced CT, the treated area displays non-enhancement on both the arterial and portal venous phase, occasionally surrounded by a penumbra which is a narrow, concentric, smooth rim of contrast enhancement that arises as a benign response to thermal injury [16]. Usually, this benign peri-tumoral enhancement resolves on subsequent imaging but can persist for up to six months [15]. The size of the ablated zone remains either stable or progressively decreases as the body removes the zone of induced coagulation and the area undergoes involution. CT scans depicting residual or recurring tumor have shown features such as general enlargement of the ablated region or nodular enhancing masses developing along the margins or near the site of ablation. Other distinctive patterns that have been correlated with tumor are unclear delineation of the margins resulting in a halo appearance and a wide, irregular peripheral enhancing rim distinguished from the adjacent hepatic parenchyma [17].

Typical MR imaging features of RFA

On typical MR imaging, the standard RFA ablation zone may appear to have low signal intensity on T2-weighted images and high signal intensity of T1-weighted images. The hypointensity on T2-weighted images is probably attributed to dehydration and coagulation as a result of the ablation process. If the ablated lesion becomes filled by fibrin or hemorrhage, a hyperintense focus may be detected on T2-weighted images. In certain cases, there is bright signal on T2-weighted imaging and contrast enhancement on T1-weighted imaging surrounding the treated lesion immediately post-treatment and this may occur from an inflammatory response to the thermal injury or reactive hyperemia. However, the fully treated area does not usually enhance on subsequent imaging. On T1-weighted imaging, lesions display heterogeneous signal intensity because necrosis patterns differ among lesions. Compared with the pre-treatment lesion, the post-ablation region is usually larger to encompass a margin of normal tissue but this area involutes over time. On follow-up imaging, recurrent or residual lesions surrounding the ablative zone appear irregular and exhibit moderately high signal intensity on T2-weighted images [18].

Materials and Methods

Patient Population

A retrospective review was performed on the records of patients with unresectable primary or metastatic liver neoplasms who underwent a Phase I clinical trial combining RFA and LTLT at our institution. Twenty-four patients were enrolled in the trial. Only 17 patients were evaluated because the remaining patients received treatment at another institution and their imaging were not available at time of evaluation. One of these patients did not have an immediate post-ablation CT scan, and was excluded from the analysis, leaving 16 for analysis. Lesion histologies included hepatocellular carcinoma, adenocarcinoma, adrenal cortical carcinoma, colorectal carcinoma, and renal cell carcinoma. Patients who underwent RFA without LTLT served as unmatched controls. These patients were obtained through

random selection of the institution's database of patients receiving RFA of a liver lesion without LTLD that had a follow-up CT scan 3 – 5 weeks later, as well as Phase I patients who had subsequent RFA performed without LTLD.

Procedure

A single dose of LTLD was given intravenously 15 minutes prior to the RFA, and the carrier liposome deployed doxorubicin at temperatures $>39.5^{\circ}\text{C}$. RFA was performed using standard algorithms with a commercial 200-W generator, and water-cooled electrodes (Covidien, Inc., Boulder, CO). All procedures were performed with patients under general anesthesia. The peri-procedural enhanced CT scan was performed immediately after the completion of treatment.

Dosing of the LTLD was implemented using the patient's body surface area (BSA in m^2) and a 3×3 dose escalation design with five dose levels: 20, 30, 40, 50, and 60 mg/m^2 .

Imaging Protocol

Serial diagnostic imaging comprised of enhanced CT, dynamic contrast enhanced MRI (DEMRI) and PET before the therapy, immediately post-procedure, at 28 ± 5 days post therapy, and at 3 month intervals (± 5 days) for the first year and then at 6 month intervals until evidence of recurrence, administration of additional antitumor treatment, or a total of 3 years. Recurrent hepatic tumors were treated with repeat RFA without LTLD after the Day 28 assessment.

Triple phase CT images were acquired on GE Lightspeed scanners (GE Healthcare, Pewaukee, WI) with Isovue-300 IV contrast. Arterial, venous, portal, and delayed phase images were obtained. MRI images were acquired on 1.5T GE Signa scanners (GE Healthcare, Pewaukee, WI). T1W, T2W pre-contrast and post-contrast MR images were obtained using gadopentetate dimeglumine (Magnevist, Bayer HealthCare, Montville, NJ) as a contrast agent.

Image analysis

All imaging scans were analyzed retrospectively by a board-certified radiologist.

Volumetric lesion size was determined on CT images by contouring the index tumors and post-treatment ablation areas on each axial slice (Vitrea, Toshiba Medical Systems, Minnetonka, MN). Penumbras were analyzed from the T1W MRI. Qualitative imaging features on CT were evaluated in terms of rim or margin enhancement characteristics, and the dynamic imaging appearances were described over time.

Case controls for patients receiving liver RFA without LTLD were compared to the study group in terms of ablation zone dynamics in the weeks following ablation.

Data Analysis

Statistical analyses were performed using JMP 9.0 (SAS Institute, Cary, NC). The change in ablation zone volume from peri-procedure imaging was compared between study subjects and controls, and was also compared between subjects receiving low ($< 40 \text{ mg}/\text{m}^2$) and high

(50 mg/m²) doses of LTLD. The presence and/or size of penumbras (regular, smooth, enhancing rim) on T1W MRI were also analyzed. The statistical testing of continuous variables was performed using the two-tailed Wilcoxon/Kruskal-Wallis rank-sum test. Statistical testing of categorical variables was performed using the Fisher's exact test. A significance level of 0.05 was used for all comparisons.

Results

Imaging from 16 patients (10 male, 6 female) in the RFA + LTLD cohort were analyzed (median age 56.5). Six control cases of standard RFA were also analyzed. Three of these cases of standard RFA were performed in different liver lesions of protocol patients that had previously undergone RFA + LTLD, and three other patients outside the protocol had undergone standard RFA at our institution (Table 1).

Qualitatively, the thermal lesion size was larger on contrast-enhanced CT 28 days after the procedure compared to peri-procedural imaging. A smooth enhancing rim was seen on contrast-enhanced CT and dynamic contrast MR imaging at the thermal lesion margin. This rim also showed hypermetabolic activity on PET imaging, and regressed over time with a benign appearance.

Tumor Size and Ablated Volumes

The mean and maximum tumor volumes for the study group and control group were 42.6 mL and 133.7 mL versus 29.0 mL and 137.4 mL, respectively (Figure 1). In one subject in the study group, two adjacent lesions were treated together; tumor size in this patient was considered to be the sum of these volumes.

In the study group, 11 of 16 (69%) had stable or increased ablative zones on CT at a mean of 29.1 days post RFA (Figure 2). Of the control group, 6 of 6 (100%) had a decrease in ablation region at a mean of 31.5 days post RFA ($p = 0.001$). At one month follow-up, the ablative zone is in fact larger in the RFA + LTLD group, and not just less quickly resolving.

At follow-up, the mean volume changes in the study group and the control group were +4.7ml and -7.4ml, which were statistically different ($p = 0.03$). When considering the change in ablation zone volume as a proportion of the peri-procedural ablation zone volume, this corresponded to a significant difference in the mean percentage change of +26.6% (median: +5.9%) and -19.1% (median: -15.5%), respectively (Figure 3, $p = 0.01$).

Within the study group alone, the change in ablative zone volume was not significantly different across dose levels of LTLD ($p = 0.65$), nor was the percentage change in ablative zone volume (Figure 4, $p = 0.40$).

3.2 Imaging Features

Distinctive imaging characteristics were found in the RFA plus LTLD group compared with conventional RFA. It was noted that one patient had a pre-existing tumor penumbra on contrast-enhanced CT and MRI and was excluded from this analysis, and in another the T1-weighted MRI was not well delineated (penumbra was measured on contrast-enhanced CT

for subsequent analysis). The follow-up T1-weighted MRI showed a regular, smooth, enhancing rim around the ablative zone in 13 of the remaining 14 cases (Figure 5). The mean and maximum volume of this penumbra was 30.5 ml and 61.4 ml. The mean and maximum volume of the penumbra as a percentage of the ablation zone size on follow-up was 53% and 125%.

Penumbra sizes of low dose vs high dose—At the lower doses of LTLD (≤ 40 mg/m²), the mean and maximum penumbra volume was 30.1 ml and 61.4 ml ($n = 8$). At high doses of LTLD (≥ 50 mg/m²), the mean and maximum penumbra volume was 30.1 ml and 48.4 ml ($n = 6$). This corresponded to a mean and maximum penumbra volume of 56% and 125% of the ablated zone in the low dose subgroup and 48% and 83% in the high dose group (Figure 6). Neither the absolute penumbra size ($p = 0.75$) nor the penumbra size as a percentage of the ablation zone were significantly different between the low dose and high dose groups ($p = 0.56$).

4. Discussion

Comparison of maximum diameters of ablative zones between the control and study groups immediately post procedure and approximately one month post procedure revealed significant differences. The ablative zones of the patients treated with RFA + LTLD were typically stable or enlarged in the four weeks following ablation, in contrast to conventional RFA where the ablative zone decreased in size in the four weeks following ablation. The mechanism of the involution has not been elucidated though there are several hypotheses. The involution may be due to stunned hypertrophy of normal liver that is impaired with ongoing cell death from chemotherapeutic mechanisms. The involution may also be attributed to atrophy of the ablated tissue from continuing coagulative necrosis. Ongoing stability or growth of the low-attenuation area of the LTLD-treated area suggests therapeutic effect at the desired ablative margin. However, the clinical significance of this is speculative.

The non-enhancing low-attenuation ablative zone on CT represents coagulation necrosis [19, 20]. The typical characteristics of a recurrent lesion include a wide rim with a nodular and irregular border [21] which is hyperdense on arterial phase [22]. The penumbra of an ablative zone after RFA treatment is often narrow, with a smooth or regular border, and decreases in enhancement over time. The addition of LTLD results in a penumbra that is usually thicker than RFA in the absence of the drug. In one study, mean lesion volumes measured by summation of areas decreased by 21%, one month after RFA, and peripheral rim enhancement on CT resolved in all 34 lesions [23]. The addition of LTLD to RFA resulted in distinctive imaging appearance of a rather wide enhancing rim but with a smooth, regular edge as evidenced by increased attenuation on CT and increased signal on MRI. Moreover, the enhancement of the treatment group appeared to persist for a longer length of time compared to that of the control group. Thus, a radiologist may potentially misinterpret the wide, persistent rim of a post RFA + LTLD region as a recurrence rather than the proposed drug effect of the LTLD. The wide enhancement seen in the imaging of the LTLD treatment group may correspond to the geometries of predicted maximum drug release at the periphery of the ablation zone, although this is speculative [11].

This analysis may potentially underestimate the sizes and characteristics of the treatment zone given that the study group was selected from a Phase I dose escalation study and thus 9 out of the 17 sample lesions were treated at drug dosages lower than the standard MTD that would generally be used for treatment. A phase III randomized clinical trial of the RFA and LTLD with doxorubicin using the MTD has recently completed and the imaging results from this study may yield a more accurate evaluation. These descriptive trends need to be validated in future studies and multi-center trials will further define imaging rules or trends for interpreting radiologists to consider.

The case controls were compiled from a database of patients treated with RFA to the liver at the same institution with the same primary operator, rather than from a prospective cohort. RFA procedures between the two groups may differ due to randomly varying techniques or patient characteristics.

The imaging features following RFA with LTLD are different from standard post-ablative imaging and can be mistaken for residual or recurrent tumor. Growth of the ablative zone after RFA with LTLD suggests ongoing drug-induced biological effects and may support a mechanism of action in this drug plus device therapy. Unlike tumor recurrence, this increase in size is expected to regress over time. Although speculative, the goal is to increase the threshold size indications for this local therapy.

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References

1. Okuwaki Y, Nakazawa T, Kokubu S, et al. Repeat radiofrequency ablation provides survival benefit in patients with intrahepatic distant recurrence of hepatocellular carcinoma. *Am J Gastroenterol*. 2009; 104:2747–2753. doi: 10.1038/ajg.2009.414. [PubMed: 19603009]
2. Aloia TA, Vauthey J-N, Loyer EM, et al. Solitary colorectal liver metastasis: resection determines outcome. *Arch Surg*. 2006; 141:460–466. discussion 466–467. doi: 10.1001/archsurg.141.5.460. [PubMed: 16702517]
3. Solbiati L, Livraghi T, Goldberg SN, et al. Percutaneous radio-frequency ablation of hepatic metastases from colorectal cancer: long-term results in 117 patients. *Radiology*. 2001; 221:159–166. [PubMed: 11568334]
4. Mulier S, Ni Y, Jamart J, et al. Local recurrence after hepatic radiofrequency coagulation: multivariate meta-analysis and review of contributing factors. *Ann Surg*. 2005; 242:158–171. [PubMed: 16041205]

5. Siperstein AE, Berber E, Ballem N, Parikh RT. Survival after radiofrequency ablation of colorectal liver metastases: 10-year experience. *Ann Surg.* 2007; 246:559–565. discussion 565–567. doi: 10.1097/SLA.0b013e318155a7b6. [PubMed: 17893492]
6. Berber E, Pelley R, Siperstein AE. Predictors of survival after radiofrequency thermal ablation of colorectal cancer metastases to the liver: a prospective study. *J Clin Oncol.* 2005; 23:1358–1364. doi: 10.1200/JCO.2005.12.039. [PubMed: 15684312]
7. Abu-Hilal M, Primrose JN, Casaril A, et al. Surgical resection versus radiofrequency ablation in the treatment of small unifocal hepatocellular carcinoma. *J Gastrointest Surg.* 2008; 12:1521–1526. doi: 10.1007/s11605-008-0553-4. [PubMed: 18592325]
8. Hong SN, Lee S-Y, Choi MS, et al. Comparing the outcomes of radiofrequency ablation and surgery in patients with a single small hepatocellular carcinoma and well-preserved hepatic function. *J Clin Gastroenterol.* 2005; 39:247–252. [PubMed: 15718869]
9. Yun WK, Choi MS, Choi D, et al. Superior long-term outcomes after surgery in child-pugh class a patients with single small hepatocellular carcinoma compared to radiofrequency ablation. *Hepatol Int.* 2010; 5:722–729. doi: 10.1007/s12072-010-9237-8. [PubMed: 21484104]
10. Petrowsky H, Busuttil RW. Resection or ablation of small hepatocellular carcinoma: what is the better treatment? *J Hepatol.* 2008; 49:502–504. doi: 10.1016/j.jhep.2008.07.018. [PubMed: 18706732]
11. Gasselhuber A, Dreher MR, Negussie A, et al. Mathematical spatio-temporal model of drug delivery from low temperature sensitive liposomes during radiofrequency tumour ablation. *Int J Hyperthermia.* 2010; 26:499–513. doi: 10.3109/02656731003623590. [PubMed: 20377363]
12. Wood BJ, Poon RT, Locklin JK, et al. Phase I study of heat-deployed liposomal doxorubicin during radiofrequency ablation for hepatic malignancies. *J Vasc Interv Radiol.* 2012; 23:248–255.e7. doi: 10.1016/j.jvir.2011.10.018. [PubMed: 22178041]
13. Thomas MB, Jaffe D, Choti MM, et al. Hepatocellular carcinoma: consensus recommendations of the National Cancer Institute Clinical Trials Planning Meeting. *J Clin Oncol.* 2010; 28:3994–4005. doi: 10.1200/JCO.2010.28.7805. [PubMed: 20679622]
14. Hong CW, Libutti SK, Wood BJ. Liposomal doxorubicin plus radiofrequency ablation for complete necrosis of a hepatocellular carcinoma. *Curr Oncol.* 2013; 20:e274–277. doi: 10.3747/co.20.1266. [PubMed: 23737698]
15. Goldberg SN, Grassi CJ, Cardella JF, et al. Image-guided tumor ablation: standardization of terminology and reporting criteria. *J Vasc Interv Radiol.* 2009; 20:S377–390. doi: 10.1016/j.jvir.2009.04.011. [PubMed: 19560026]
16. Nghiem HV, Francis IR, Fontana R, et al. Computed tomography appearances of hypervascular hepatic tumors after percutaneous radiofrequency ablation therapy. *Curr Probl Diagn Radiol.* 2002; 31:105–111. [PubMed: 12140514]
17. Schima W, Ba-Ssalamah A, Kurtaran A, et al. Post-treatment imaging of liver tumours. *Cancer Imaging.* 2007; 7(Spec No A):S28–36. doi: 10.1102/1470-7330.2007.9047. [PubMed: 17921098]
18. Vossen JA, Buijs M, Kamel IR. Assessment of tumor response on MR imaging after locoregional therapy. *Tech Vasc Interv Radiol.* 2006; 9:125–132. doi: 10.1053/j.tvir.2007.02.004. [PubMed: 17561215]
19. Solbiati L, Goldberg SN, Ierace T, et al. Hepatic metastases: percutaneous radio-frequency ablation with cooled-tip electrodes. *Radiology.* 1997; 205:367–373. [PubMed: 9356616]
20. Goldberg SN, Gazelle GS, Mueller PR. Thermal ablation therapy for focal malignancy: a unified approach to underlying principles, techniques, and diagnostic imaging guidance. *AJR Am J Roentgenol.* 2000; 174:323–331. doi: 10.2214/ajr.174.2.1740323. [PubMed: 10658699]
21. Gazelle GS, Goldberg SN, Solbiati L, Livraghi T. Tumor Ablation with Radio-frequency Energy. *Radiology.* 2000; 217:633–646. [PubMed: 11110923]
22. Catalano O, Esposito M, Nunziata A, Siani A. Multiphase helical CT findings after percutaneous ablation procedures for hepatocellular carcinoma. *Abdom Imaging.* 2000; 25:607–614. [PubMed: 11029093]
23. Lim HK, Choi D, Lee WJ, et al. Hepatocellular carcinoma treated with percutaneous radio-frequency ablation: evaluation with follow-up multiphase helical CT. *Radiology.* 2001; 221:447–454. [PubMed: 11687689]

Figure 1. Sizes of index lesions, peri-procedural ablation zones, and ablation zones at one month follow-up in the RFA + LTLD and RFA alone groups.

Figure 2.

Imaging of a patient treated with RFA + LTLD. Volumes were contoured (red areas) on CT imaging prior to ablation (A1), immediately after ablation (A2), and at follow-up after one month (A3). Corresponding volumetric representation of tumor size (B1) and ablative zones (B2 and B3) are shown as well.

Figure 3.

The percentage change in ablative zone volumes at one-month follow-up from periprocedural imaging is compared between the control and study groups.

Figure 4.

The percentage change in ablative zone volumes at one-month follow-up from periprocedural imaging is compared between the control group and various dosage levels of LTLD.

Figure 5. Smooth hyper-enhancing rim (black arrow) surrounding the ablative zone on follow-up T1W imaging (a). Penumbra volumes measured by contouring the rim on axial slices (b).

Figure 6. Penumbra size as a percentage of the ablation zone size in the low dosage (40 mg/m² of LTLD) and high dosage (50 mg/m² of LTLD) groups.

Table 1

Characteristics of the RFA + LTLD and conventional RFA cases performed

Characteristic		RFA + LTLD (n = 16)	RFA alone (n = 6)
Age (Mean $\pm$ SD)		57.9 $\pm$ 13.8	54.5 $\pm$ 13.7
Gender	Male	10 (62.5%)	1 (16.7%)
	Female	6 (37.5%)	5 (83.3%)
Index tumor size (Mean $\pm$ SD/ml)		42.6 $\pm$ 40.5	29.0 $\pm$ 53.9
Peri-procedural ablation zone size (Mean $\pm$ SD/ml)		59.7 $\pm$ 43.0	53.0 $\pm$ 55.2
Ablation zone size at one-month follow-up (Mean $\pm$ SD/ml)		64.4 $\pm$ 43.7	45.6 $\pm$ 52.9
Change in ablation zone size	Increased or stable	11 (68.8%)	0 (0%)
	Regressed	5 (31.3%)	6 (100%)
Absolute change in ablation zone size (Mean $\pm$ SD/ml)		+4.7 $\pm$ 24.4	-7.4 $\pm$ 4.0
Percentage change in ablation zone size (Mean $\pm$ SD)		+26.6 $\pm$ 59.3%	-19.1 $\pm$ 13.0%