Review Article

Local radiation for cutaneous T-cell lymphoma other than mycosis fungoides and Sézary syndrome

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Abstract: Primary cutaneous lymphoma is the second most common type of extranodal lymphoma. The clinical behavior of this lymphoma differs from that of other extranodal lymphomas and thus requires a particular pretreatment evaluation and treatment strategy. Cutaneous T-cell lymphoma (CTCL) accounts for 80% of primary cutaneous lymphoma cases and includes several confirmed disease entities as well as provisional entities. Local radiation for CTCLs is applicable for both curative and palliative intents and is based on the involved-site radiotherapy (ISRT) concept. Primary cutaneous CD30-positive lymphoproliferative disorders include primary cutaneous anaplastic large-cell lymphoma (C-ALCL), lymphomatoid papulosis (LyP), and borderline lesions, all of which exhibit indolent behavior. One half of all LyP cases show spontaneous regression and do not require active treatment. Solitary or localized C-ALCL cases are treated with surgical excision or local radiation of 24–36 Gy. The most common relapse site after local treatment is other skin areas; however, skin relapse is not associated with worsened prognosis. Subcutaneous panniculitis-like T-cell lymphoma (SPTL) without hemophagocytic syndrome exhibits indolent behavior, and localized lesions can be successfully treated with local radiation of 40 Gy or more. Extranodal NK/T-cell lymphoma, nasal type has an aggressive clinical behavior even with intensive chemotherapy and a dose of 50 Gy or higher might be required for good tumor control. Palliative local radiation of 8 Gy in one or two fractions is effective in treating refractory or relapsed CTCLs. ISRT with curative intent should encompass the original suspicious lesions plus a 2–3 cm margin, while ISRT with palliative intent should encompass visible lesions plus a 1–2 cm margin. Appropriate electron beam energy and bolus thickness should be selected according to the skin surface dose and thickness of the patch and plaque lesions. All CTCL cases should be reviewed by a multidisciplinary team to ensure an appropriate treatment strategy.

Keywords: Cutaneous T-cell lymphoma (CTCL); CD30-positive lymphoproliferative disorders; subcutaneous panniculitis-like T-cell lymphoma (SPTL); extranodal NK/T-cell lymphoma; nasal type; local radiation

Submitted May 19, 2018. Accepted for publication Jun 28, 2018.
doi: 10.21037/cco.2018.07.01
View this article at: http://dx.doi.org/10.21037/cco.2018.07.01

Introduction

Primary cutaneous lymphoma is the second most common type of extranodal lymphoma, and is defined as a hematological neoplasm present in the skin with no evidence of extra-cutaneous disease at the time of diagnosis (1). It exhibits significantly different clinical behavior and prognosis from those of extranodal lymphomas with origins other than the skin, and each requires a particular treatment strategy. Primary cutaneous T-cell lymphoma (CTCL) occurs most frequently in patients in their 60s to 80s (predominantly in males) and accounts for 71–87% of primary cutaneous lymphomas (2-4). The Surveillance, Epidemiology, and End Results (SEER) program deems that CTCL incidence is 10 per million persons, the proportion of which has been stable since 1998 (2). The World Health

Organization (WHO) and the European Organization for Research and Treatment of Cancer (EORTC) reported new classification for primary cutaneous lymphomas in 2005, and the disease concepts of primary cutaneous lymphoma have been dramatically reorganized since then (1). CTCL cases primarily comprise those involving mycosis fungoides, Sézary syndrome, primary cutaneous CD30-positive lymphoproliferative disorders, subcutaneous panniculitis-like T-cell lymphoma (SPTL), extranodal NK/T-cell lymphoma, nasal type (ENKTCL), adult T-cell lymphoma, and primary cutaneous peripheral T-cell lymphoma, unspecified (PTCL-NOS). The 2016 revision of the WHO classification of lymphoid neoplasms added two provisional disease entities of CTCLs (5). Over the past decade, the international consensus of staging classification, clinical endpoints and response criteria, and treatment guidelines for CTCLs have been reported, and basic systems to establish a standard of care for CTCLs have progressed (1,6-14). Local radiation for CTCLs has been applied with both curative and palliative intents in clinical practice (15). The aim of this article is to clarify the utility of local radiation for CTCLs other than mycosis fungoides and Sézary syndrome as part of a multidisciplinary treatment strategy.

Pretreatment evaluation

Biopsies of all types (punch, incisional, or excisional biopsy) of suspicious skin lesions aid in the final diagnosis, and all specimen slides should be reviewed by experienced hematopathologists or dermatopathologists (16). Re-biopsy should be considered if the histopathological specimen is insufficient to make a final diagnosis. Adequate immunohistochemistry panels for final diagnosis may include CD2, CD3, CD4, CD8, CD20, CD30, CD56, anaplastic lymphoma kinase, BCL6, Ki-67, and other typing panels (16). Clonal T-cell receptor gene rearrangement including alpha/beta (α/β) and gamma/delta (γ/δ) chains is essential for making a final diagnosis and deciding on a treatment strategy (1).

The International Society for Cutaneous Lymphomas (ISCL) and EORTC revised the TNMB staging system and classification for mycosis fungoides and Sézary syndrome in 2007 (17). They also proposed a separate TNM staging system for CTCLs other than mycosis fungoides and Sézary syndrome (12). All patients should undergo the appropriate staging procedures, which include obtaining a medical history, complete physical examination including peripheral lymph node regions, liver and spleen enlargement, complete skin examination by a dermatologist, complete blood count with differential white blood cell count, serum biochemistry including lactate dehydrogenase, and imaging evaluation (9,11,16,17). Standardized photographs are recommended for documentation of the appearance of skin lesions at baseline and during disease progression (11). Contrast-enhanced computed tomography (CT) of the chest, abdomen, and pelvis is routinely undertaken for patients with T3–4 disease to assess nodal and visceral involvement, but has limited value for patients with T1–2 disease (13,18). However, unlike mycosis fungoides, PTCL-NOS does not follow the typical progression process through localized patch and plaque disease via tumor-stage disease and finally to generalized and/or disseminated disease. Instead, PTCL-NOS is more likely to present as widespread plaque disease coexisting with tumor-stage disease from the onset (19). Integrated whole body fludeoxyglucose (^{18}F) positron emission tomography and CT are recommended for patients with primary cutaneous anaplastic large-cell lymphoma (C-ALCL) and more aggressive CTCLs such as ENKTCL and PTCL-NOS (16,20). Bone marrow aspiration and biopsy have limited value for patients with C-ALCL, but may prove to be informative for patients with ENKTCL and PTCL-NOS. Examination of the ear, nose, and throat should be taken into consideration for patients with ENKTCL (16).

Local radiation for primary cutaneous CD30-positive lymphoproliferative disorders

Primary cutaneous CD30-positive lymphoproliferative disorders are the second most common type of CTCLs, and account for 14–30% of all CTCLs (1,4). This particular type consists of C-ALCL, lymphomatoid papulosis (LyP), and borderline lesions (10,21). These disease entities occur on a continuous disease spectrum ranging from benign LyP to malignant C-ALCL, with substantial overlap between entities (21-24). Histological differentiation between C-ALCL and LyP is difficult, and clinicopathological correlation is critical to make an accurate diagnosis (25,26). History and evidence of other CTCLs should be evaluated at the initial diagnosis (25,27). C-ALCL is defined as a CTCL composed of anaplastic large cells with expression of CD30 in more than 75% of tumor cells (28). C-ALCL usually appears on the extremities, trunk, and head and neck, and affects middle-age and elderly patients (predominantly males) (21,23,28-30). Eighty percent of patients with C-ALCL have solitary or localized lesions, and 20% have generalized skin lesions (31). Extra-

cutaneous involvement occurs in approximately 10% of patients with C-ALCL, and tends to affect regional lymph nodes (21). Spontaneous regression ranging from 6 to 22% has been observed in patients with C-ALCL, and remaining lesions and regrowth lesions require active treatment (26,32). For solitary and localized C-ALCL, waiting for spontaneous regression, surgical excision, or local radiation represent first-line treatment options, while postoperative radiation may be considered for those with insufficient surgical margins (24,27,32). Although C-ALCL exhibits indolent behavior, localized involvement of the extremities with multiple lesions is known as "extensive limb disease" and is associated with poor outcomes (32). Patients with multiple or disseminated disease are treated with low-dose methotrexate, but intensive multi-agent chemotherapy is not usually recommended (28).

LyP usually occurs in middle-age patients but can also occur occasionally in elderly patients and children, on the trunk and extremities (21). Eighty percent of LyP cases show generalized skin lesions, with the remaining 20% showing localized skin lesions at presentation (24,33). LyP has a histological appearance of a malignant disease, but exhibits clinically benign behavior (21). LyP is histologically heterogeneous with several histologic subtypes (types A to D, among others) (1,32,33). One half of LyP cases show spontaneous regression within weeks to months; these cases do not require active treatment (2,21,27,32-34). Ten to 61% of patients with LyP develop or have coexisting hematologic malignancies including systemic anaplastic large cell lymphoma, mycosis fungoides, or Hodgkin's lymphoma (26,27,34). Furthermore, 10% of patients with LyP have an increased risk of non-hematologic malignancies (35). Topical therapies and phototherapy provide early clinical response, but do not prevent the development of new lesions on the skin outside of the treated area (32,34). No treatment has been developed that effectively influences the natural course of LyP, and the short-term benefits of active treatment should be balanced carefully with potential long-term adverse effects (1). Localized LyP could be treated with close observation, topical steroids, and phototherapy as first-line treatment (16,24). Close observation without radiation is an important strategy to prevent the development of secondary malignancies in patients with LyP (32). Phototherapy, surgical excision, or local radiation may be recommended as alternatives to observation for LyP lesions larger than 2 cm in diameter which persist for months without spontaneous regression (10,24). For generalized LyP lesions, close observation, low-dose methotrexate (5–20 mg per week), phototherapy, systemic retinoids, topical steroids, or topical mechlorethamine have been reported (16,32,33).

In 2011, the EORTC, ISCL, and United States Cutaneous Lymphoma Consortium (USCLC) reported an optimal radiation dose of 30–46 Gy for C-ALCL (10). However, one study of a Dutch registry of primary cutaneous lymphomas and one from the MD Anderson Cancer Center recently reported that there was no definite dose-response relationship for C-ALCL (30,31). The former recommended 20 Gy in 8 fractions as the optimal regimen, while the latter recommended conventional fractionated radiation of 30 Gy or less. The International Lymphoma Radiation Oncology Group (ILROG) analyzed 56 patients recruited from the 8 collaborating institutions and reported a recommended dose of 30 Gy for good local control (29). The National Comprehensive Cancer Network (NCCN) Clinical Practice Guideline in Oncology (version 3. 2018) recommended a total dose of 24–36 Gy for C-ALCL (16). On the other hand, small case-series studies have applied fractionated radiotherapy of 30–45 Gy in 2–2.5 Gy fractions or a single fraction of 7.5–8 Gy for LyP (22,36).

In most patients with localized C-ALCL, surgical resection or local radiation results in a complete response and excellent tumor control (23,25,27-29). Smith and colleagues reported that only 70% of patients achieved a complete response within the first 3 months after local radiation, but that after long-term follow-up most patients achieved excellent tumor control (30). Long-term careful observation after local radiation might be required to avoid over-treatment. Relapse rates after initial local treatment range from 30% to 64%, with a median disease-free survival time of only 16 months (23,25-27,32,37). The most common relapse site after local treatment is other skin areas (the same anatomic area as the initial lesion), while the next most common relapse site is the regional lymph node area (1,23,27,30,32,37). Cutaneous relapse after local treatment is not associated with worsened prognosis. Ten-year disease-specific survival rates of patients with localized C-ALCL range from 90–98%, with a 5-year disease-specific survival rate of approximately 50% among patients with generalized lesions (1,26,28,29,34).

In a recent multicenter retrospective analysis of 252 patients with LyP, complete response to first-line treatment including topical steroids, low-dose methotrexate, and phototherapy was achieved in only 48% of patients (33). Of those who achieved a complete response, 78% developed cutaneous relapse with a median disease-free survival of

only 11 months (33). Type A lesions and use of first-line treatments other than phototherapy were associated with early cutaneous relapse. In spite of high cutaneous relapse rates after first-line treatment, LyP patients have excellent prognoses, with 5-year overall survival rates of 98–100% (1,32,34). Only 4% of patients with LyP developed systemic disease, and only 2% reportedly died of systemic disease within the median follow-up period of 6 years (1,27). Regular, long-term follow-up is important to monitor development of second lymphoid and non-lymphoid malignancies (16). Patients with borderline lesions tend to develop C-ALCL more readily than patients with LyP, but the treatment outcome is favorable (21).

Local radiation for SPTL

SPTL is an extremely rare disease, accounting for approximately 2% of CTCL cases in Japan (4). According to the SEER program, SPTL affects middle-aged (median age, 47 years) individuals, predominantly female (67%) (38). Previously, confusion surrounded the disease entity of SPTL until the new WHO-EORTC classification was reported in 2005. Currently, the term "SPTL" is only used for patients with α/β T-cell phenotype (1,39,40). CTCLs with γ/δ T-cell phenotype should be excluded from the current definition. SPTL with α/β T-cell phenotype generally presents as a CD4–, CD8+, CD56–, and βF1+ phenotype, and is uncommonly affiliated with hemophagocytic syndrome (17–32%) (40,41). Patients show nodular skin lesions and deeply seated plaques, and half of them complain of fever, chills, night sweats, fatigue, and anorexia (24,39,40). Most patients have generalized skin lesions in the extremities and trunk, and approximately 20% of patients have solitary or localized skin lesions. SPTL without hemophagocytic syndrome exhibits indolent behavior and excellent prognosis relative to that of SPTL with hemophagocytic syndrome (5-year overall survival: 91% *vs.* 46%, respectively) (9,40). Hemophagocytic syndrome is often associated with aggressive clinical behavior, and patients should be treated with intensive multi-agent chemotherapy (1,9,13,40,41). Other unfavorable prognostic factors for overall survival of patients with SPTL include old age (>65 years) and disseminated disease (38). Solitary or localized lesions of SPTL without hemophagocytic syndrome may be treated with local radiation alone (9,39,40,42). CTCLs with γ/δ T-cell phenotype present as a CD4–, CD8–, CD56+/–, βF1+ phenotype, and are often affiliated with hemophagocytic syndrome and aggressive behavior (1,39,40). Most patients with γ/δ T-cell phenotype have generalized lesions in the extremities and trunk, with approximately 30% of them displaying general symptoms and/or hepatosplenomegaly (40). Patients with γ/δ T-cell phenotype are treated with intensive multi-agent chemotherapy, but the clinical response to chemotherapy has been disappointing (41). Systemic relapse has been observed in the lungs, liver, kidneys, and central nervous system, and high-dose chemotherapy and stem cell transplantation have been investigated (41).

Although there is little information on the optimal radiation dose for SPTL, the European Society for Medical Oncology (ESMO) and ILROG recommend high-dose radiation of 40 Gy or more (8,42). In one study, after initial treatment, half of those with α/β T-cell phenotype developed new skin lesions outside the irradiated areas, but none developed extra-cutaneous involvement (40). Kong and colleagues reported that approximately half of their patients showed complete or partial responses after multi-agent chemotherapy (39). The 5-year overall survival rate of patients with current SPTL might be more than 80%, while that of patients with γ/δ T-cell phenotype is only 11% (1,9,38-40).

Local radiation for extranodal NK/T-cell lymphoma, nasal type (ENKTCL)

ENKTCL is nearly always Epstein-Barr virus-related lymphoma, and is relatively common in Asia, Central America, and South America (1,21,42). A nationwide survey by the Japanese Skin Cancer Society Lymphoma Study Group found that among 1,733 patients with primary cutaneous lymphomas, the incidence of ENKTCL was 2.3% (4), which was higher than that in Western countries (<1%), but lower than that in Korea (20%). Multiple subcutaneous nodules with or without necrosis are found in the extremities, head and neck, and trunk (21,43). ENKTCL shows CD56 positivity, and exhibits aggressive clinical behavior and poor survival rates (9,21,43). Although intensive multi-agent chemotherapy could be applied, resistance to anthracycline-containing chemotherapy is common (43). Patients with advanced disease could be treated with platinum-based chemotherapy with or without local radiation, but thus far, treatment outcomes have been disappointing (1,13).

High-dose radiation to the primary site might be required for good tumor control, but the role of local radiation has not been clarified for patients with generalized

ENKTCL lesions. The NCCN Clinical Practice Guideline recommends a radiation dose of 45–50.4 Gy when combination therapy is applied, and 50 Gy or higher with radiotherapy alone (16). ILROG and ESMO recommended a dose of 50 Gy to the initial lesion followed by boost irradiation of 5–10 Gy to residual lesions (8,42). Median survival time of patients with cutaneous localized lesions is 27 months, and that of patients with extra-cutaneous disseminated lesions ranges from 5 to 10 months (1,43).

Local radiation for primary cutaneous peripheral T-cell lymphoma, unspecified (PTCL-NOS)

PTCL-NOS is a heterogeneous group that includes CTCL types that do not fit into any of the better defined subtypes of the WHO-EORTC classification; it also includes several ill-defined provisional subtypes (1,21). A careful clinical history and accurate clinical examination are required to rule out transformed mycosis fungoides and other CTCLs (28). PTCL-NOS accounts for 6.7% of CTCLs in Japan (4). Each provisional subtype accounts for less than 1% of CTCLs, and their clinical behaviors have not been clarified. PTCL-NOS generally presents with an aggressive clinical behavior and poor survival rate, and commonly occurs in adults (1,9). Primary cutaneous aggressive epidermotropic CD8+ T-cell lymphoma and cutaneous γ/δ T-cell lymphoma present with progressive behavior, and even patients with solitary or localized lesions rapidly develop widespread disease (1,44). Primary cutaneous aggressive epidermotropic CD8+ T-cell lymphoma has localized or disseminated lesions with ulceration, hemorrhage, and necrosis, and tends to disseminate to other visceral organs including the lungs, testes, oral cavity, and central nervous system, but generally spares the lymph nodes (19). CD8 positivity itself is not associated with a poor prognosis, and among CD8-positive patients with mycosis fungoides variant, C-ALCL and other CTCLs exhibit indolent behavior (45). Discerning between primary cutaneous aggressive epidermotropic CD8+ T-cell lymphoma and other CD8-positive CTCLs is critical in order to avoid overly aggressive treatment. Furthermore, the 2016 revision of the WHO classification of lymphoid neoplasms proposed "Primary cutaneous acral CD8+ T-cell lymphoma" as a provisional entity; this lymphoma exhibits indolent clinical behavior (5).

Primary cutaneous γ/δ T-cell lymphoma presents as generalized skin lesions on the extremities (1,21). Intensive systemic chemotherapy can be applied, but the clinical response has been disappointing (44,46). Allogeneic stem cell transplantation can be considered for some cases, but little information is available on anticipated outcomes (42).

Half of the patients with primary cutaneous CD4+ small/medium-sized pleomorphic T-cell lymphoma have solitary or localized skin lesions, and others have multifocal lesions (44,47). Those with a solitary lesion and low proliferative index (Ki-67 <10%) can expect excellent outcomes after local radiation or surgical excision (42,44,47). For patients with disseminated disease, intermediate levels of aggression are observed, and relapse and progression to the lymph nodes and visceral organs can develop after multi-agent chemotherapy (21). Primary cutaneous CD4+ small/medium-sized pleomorphic T-cell lymphoma with a high proliferative index (Ki-67 >20%) and/or bulky tumors exhibit aggressive clinical behavior (47). Differential diagnosis between the two types of primary cutaneous CD4+ small/medium-sized pleomorphic T-cell lymphomas is critical for planning an appropriate treatment strategy.

ILROG reported that a clinical response for primary cutaneous γ/δ T-cell lymphoma after conventional fractionated local radiation of 24–30 Gy may be possible, but that it tends to relapse at the same site (8,46). Pedretti and colleagues treated 10 patients with primary cutaneous γ/δ T-cell lymphoma using 30–40 Gy (median, 36 Gy), and found that 3 patients developed local relapses at the same site (46). The NCCN Clinical Practice Guideline provides general radiation dose guidance for peripheral T-cell lymphoma arising from any site, and recommends a consolidation dose for complete response after chemotherapy of 30–36 Gy, a complementary dose for partial response of 40–50 Gy, and a dose of 40–55 Gy for primary treatment of non-candidates for chemotherapy or as salvage treatment for refractory disease (16).

Median survival times of patients with primary cutaneous aggressive epidermotropic CD8+ T-cell lymphoma and cutaneous γ/δ T-cell lymphoma are 32 months and 15 months, respectively (1,21). Patients with primary cutaneous CD4+ small/medium-sized pleomorphic T-cell lymphoma have a relatively favorable prognosis, with 5-year overall survival rates of 75% (1). Among patients with small/medium-sized pleomorphic T-cell lymphoma, those with a CD4-positive phenotype are likely to have a good prognosis relative to those with a CD4-negative phenotype (44).

Palliative local radiation for refractory or relapsed CTCL

Short-course local radiation is an effective palliative therapy

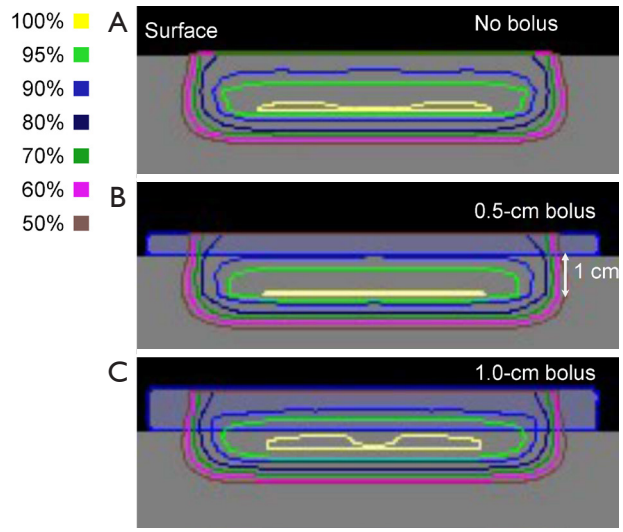

Figure 1 Dose distribution using 6 MeV electron beams with/without bolus on smooth surface site of rectangular phantom. (A) Surface dose is approximately 80% (without bolus); (B) Bolus of 0.5-cm thickness improves the surface dose to approximately 90%; (C) Bolus of 1-cm thickness improves the surface dose to approximately 100%.

for refractory or relapsed CTCLs (22,48-50). Although the clinical response after 4 Gy in 2 fractions is only 30% and remission time is very short for symptomatic CTCLs, symptom relief after 8 Gy in 1 or 2 fractions is favorable, with a complete response rate over 90% and a mean remission time for relapse of approximately 9 months (8,48,49,51). Bulky tumors may require a higher dose (8). For primary cutaneous CD30-positive lymphoproliferative disorders, a single fraction of 7.5–8 Gy results in a 100% complete response rate and long remission (22). Thomas and colleagues analyzed 58 patients with CTCLs (mycosis fungoides in 47 patients; LyP in 4; cutaneous γ/δ T-cell lymphoma in 3; Sézary syndrome in 3) who were treated by a single fraction of palliative radiation, and reported a complete response rate of 94% after a single fraction of 7–8 Gy (49). However, the clinical response of CD4-negative lesions after local radiation was disappointing (40–50%) when compared to that of CD4-positive lesions (49). Small case-series studies found complete response rates ranging from 50% to 100% after 6–8 Gy in 2–4 Gy fractions (52,53). Initial radiation doses of 8 to 12 Gy will allow re-irradiation, although a smaller fraction size of 3–5 Gy might be preferred for re-irradiation (8). Fractionated radiation should be considered in cases involving a large radiation field (8,34). The appropriate palliative radiation dose for ENKTCL has not been clarified, but high-dose radiation might be required to obtain good symptom relief and tumor control.

Technical aspects of local radiation

Local radiation for primary cutaneous lymphoma is based on the ISRT concept, which minimizes the prophylactic irradiated area without compromising treatment outcome (16). It spares adjacent uninvolved organs such as lungs, bone, and muscle. Clinical target volume (CTV) for patients with patch and/or plaque disease should encompass the epidermis and dermis, and that for patients with tumor lesions should encompass the tumor extension (34,54). The lateral field margin of definitive local radiation can be limited to 2–3 cm beyond the pretreatment defined lesion and suspicious area (8,34,55). For palliative radiotherapy, CTV will encompass the visible lesion with a margin of 1–2 cm of surrounding healthy-looking skin (8,48). Appropriate electron beam energy should be selected for the skin surface dose and thickness of patch and plaque lesions, and photon beams could be considered for tumor lesions. A daily bolus of 0.5–1 cm thickness is used to prescribe to the 80–90% isodose line to cover each lesion (55) (*Figure 1*).

A single radiation field of electron beam is desirable from the viewpoint of homogeneous dose distribution, but the multiple-field technique is required at complex anatomical sites such as the face, axilla, and breast, and at convex surface sites such as the scalp and extremities. If the multiple-field technique using electron beams is applied, then the junction of abutting fields should be shifted frequently during the course of treatment to avoid over-dose and under-dose in these areas (*Figure 2A*). A novel radiotherapy technique called helical intensity-modulated radiation therapy (helical IMRT), using 6 MV photons and binary collimators, might be useful for obtaining homogeneous dose distribution at complex anatomical sites and convex surface sites (*Figure 2B*). The advantages of helical IMRT are (I) homogeneous dose distribution to the skin and subcutaneous area, (II) irregular-shaped radiation field to avoid risk organs, and (III) sparing of deep structures such as bone marrow and visceral organs. Meanwhile, disadvantages include the (I) complex technique and (II) inconvenience of plan modification upon tumor shrinkage. Another radiation technique using photon beams with rice packing for tissue compensation could be applicable for highly irregular surface sites such as the

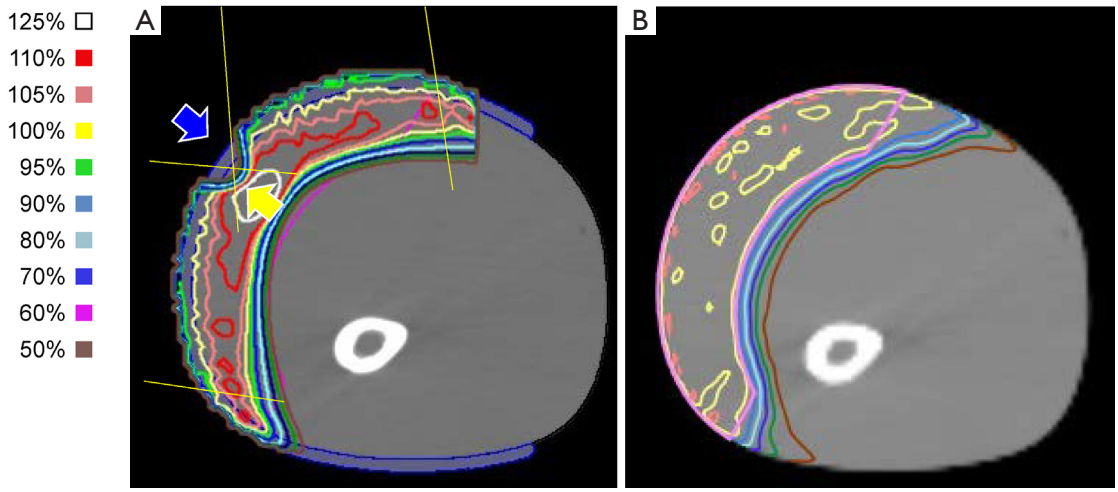

Figure 2 Dose distribution on convex surface of lower limb phantom by the multiple-field technique of electron beams and helical intensity-modulated radiation therapy (helical IMRT). (A) Multiple-field technique using 9 MeV electron beams creates low-dose and over-dose areas in the junction of abutting fields. Blue arrow: low-dose area on the skin surface. Yellow arrow: high-dose area in the subcutaneous area. (B) Helical IMRT using 6 MV photons and bolus is able to deliver homogeneous dose distribution over a large convex surface area. High-dose areas of more than 110% are not shown.

entire foot (including digits) (56). The advantages of the rice packing technique include the (I) simple work process and (II) homogeneous dose distribution regardless of tumor shrinkage. Disadvantages include the (I) high radiation dose to deep structures, (II) difficulty of creating an irregular-shaped radiation field to avoid irradiation of risk organs, and (III) applicational difficulty for head and neck irradiation. A small case-series study reported the utility of a brachytherapy technique for CTCL lesions arising from convex surfaces such as the hands or feet (50).

Conclusions

All patient cases should be reviewed by a multidisciplinary team to ensure the selection of an appropriate treatment strategy based on histological subtype, staging evaluation, clinical features, and patient condition. Further prospective and retrospective studies and a large-scale registry database are required to establish the standard of care for CTCLs.

Acknowledgements

I would like to thank Mr. K. Usui for his technical support. *Funding*: This work was supported by a Grant-in-Aid for Cancer Research from the Ministry of Health, Labour and Welfare of Japan (29-A-3).

Footnote

Conflicts of Interest: The author has no conflicts of interest to declare.

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Cite this article as: Shikama N. Local radiation for cutaneous T-cell lymphoma other than mycosis fungoides and Sézary syndrome. Chin Clin Oncol 2019;8(1):8. doi: 10.21037/cco.2018.07.01

