Total skin helical tomotherapy based on 3D printed total skin bolus

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Abstract

Objective

To investigate the effectiveness of the 3D printing total skin bolus which was first used to treat mycosis fungoides (MF) with total skin helical tomotherapy (TSHT).

Materials and Methods

A 65-year-old female MF patient with a 3-year medical history was studied, and an in-house desktop fused deposition modeling printer was used to make flexible material of 5 mm thickness for the total skin bolus to increase the skin dose through build-up. The patient was scanned in upper and lower segments while the position of 10cm above the patella was defined as the dividing line, the prescription was 24 Gy in 24 fractions, and 5 times per week. The plan parameters consisting of the FW of 5 cm, the pitch of 0.287 and the MF of 3. The complete block was 4 cm away from the planning target volume (PTV) to reduce the dose of the internal organ at risk (OAR) especially the total bone marrow. Cheese Phantom point dose, ArcCHECK 3D plane dose, and total body multi-point EBT3 film verification was performed to ensure dose delivery accuracy. Finally, MVCT guidance was used to ensure the accuracy of setup and treatment.

Results

A 5 mm thick 3D printing suit was used as the bolus to achieve target volume coverage with 95% of the prescribed dose. The lower target's conformity index (CI) and homogeneity index (HI) were slightly better than the upper target. The doses of bone marrow gradually decreased with increasing distance from the skin, and the doses of other OARs were within the clinical requirements. The deviation of point dose verification was less than 1%, the 3D plane dose verification was greater than 90%, and the film multi-point dose verification deviation was less than 3%, multiple verification methods have proved the accuracy of the actual dose. The total treatment time was about 1.5 hours (0.5 hour for wearing 3D printing suit and 1 hour for beam-on), and patients may only have slight fatigue, mild nausea or vomiting, low-grade fever, and grade bone marrow suppression.

Conclusion

The TSHT of 3D printing suit can produce a uniform dose distribution with a short treatment time, simple implementation process, good clinical effect, and low toxic effect, this study provides one more treatment method to reach a better clinical effect for the treatment of MF.

Introduction

MF is the most common type of Cutaneous T-cell lymphomas which accounts for nearly 50%, and the prognosis can reach 87% in 5 years[1]. MF usually has a high degree of radiosensitivity for radiotherapy (RT), and RT plays an important role in the treatment[2]. Total skin electron irradiation (TSEI) is the traditional treatment method, which is also clinically regarded as one of the most effective methods for MF[3]. At present, the dual-frame six-field irradiation technology developed by the Stanford University School of Medicine was widely used, however, the long treatment distance requires the patient to stand and perform multi-field irradiation with a rotating gantry, which is a burden for the patient[4]. With the emergence of helical tomotherapy (HT)[5], which unique components endows HT with many advantages, especially the ability to treat ultra-long target (160 cm × 40 cm) in a single session, it is very suitable for the treatment of long and complex target, such as total body multiple metastatic irradiations, craniospinal irradiation, total body irradiation, total marrow irradiations, etc.[6]. Moreover, the traditional TSEI required patients to stand all the time during treatment, while the lying down treatment method of TSHT makes patients less fatigue, more comfortable and better dose distribution. Hsieh CH et al.[7] was the first to use 3 mm diving suit as bolus to perform TSHT. To increase the skin dose by changing the bolus. Deveau MA et al.[8] used 3D printing technology to create the dog's total skin bolus for TSHT. Baltz GC et al.[9] used 3D printing technology to make total scalp bolus to achieve total scalp irradiation. So far there is no report about TSHT of MF using total skin bolus by 3D printing technology. The purpose of this work is to use 3D printing technology to make thermoplastic urethane (TPU) suit to perform TSHT, in order to provide one more treatment method and better clinical effects for the treatment of MF.

Results

Comparisons Of Dosimetric Parameters Of Target Volumes
Table 1
PTV mean, HI, and CI of the upper segment target and the lower target including four sub-targets (Gy, x ± s)

<table>
<thead>
<tr>
<th>site/result</th>
<th>PTV_{mean}(Gy)</th>
<th>HI</th>
<th>CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lower</td>
<td>24.92 ± 1.65</td>
<td>1.10</td>
<td>0.89</td>
</tr>
<tr>
<td>Upper</td>
<td>25.48 ± 1.98</td>
<td>1.14</td>
<td>0.75</td>
</tr>
<tr>
<td>Upper_Head&amp;Neck</td>
<td>25.45 ± 1.23</td>
<td>1.12</td>
<td>N/A*</td>
</tr>
<tr>
<td>Upper_Thorax&amp;Abdomen</td>
<td>25.82 ± 1.31</td>
<td>1.13</td>
<td>N/A*</td>
</tr>
<tr>
<td>Upper_Arm_L</td>
<td>25.33 ± 2.03</td>
<td>1.38</td>
<td>N/A*</td>
</tr>
<tr>
<td>Upper_Arm_R</td>
<td>25.43 ± 2.10</td>
<td>1.34</td>
<td>N/A*</td>
</tr>
</tbody>
</table>

* There is no corresponding \( V_{ref} \) for the sub-targets, so there is no CI result here.

The plans of the upper and lower segment target were separately designed. The upper segment target was long and complex, to ensure that each part of the upper segment target meets clinical requirements, it was divided into four parts including head and neck, thorax and abdomen, left arm, and right arm, the result can be observed from Table 1. In contrast, the lower segment target is closer to the prescription dose than the upper segment target, while the CI and HI of the lower segment target are slightly better than the upper segment target from transverse, coronal and sagittal plane dose distribution (Fig. 1).

Comparisons Of Dosimetric Parameters Of Auxiliary-structure

Table 2
Statistical of OARs dose (Gy, x ± s)

<table>
<thead>
<tr>
<th>OARs</th>
<th>Bone_Leg</th>
<th>Bone_H&amp;N</th>
<th>Bone_Pelvis</th>
<th>Bone_Spinal</th>
<th>Bone_Rib</th>
<th>Bone_Arm</th>
<th>Bone_Femer</th>
<th>Parotid_L</th>
</tr>
</thead>
<tbody>
<tr>
<td>( D_{mean}/D_{max} )</td>
<td>5.99 ± 4.68/29.82</td>
<td>18.03 ± 9.58/30.22</td>
<td>6.84 ± 6.41/30.09</td>
<td>3.46 ± 1.46/16.41</td>
<td>9.52 ± 8.77/30.16</td>
<td>21.16 ± 5.68/30.45</td>
<td>3.57 ± 0.43/6.27</td>
<td>25.07 ± 5.81/29.94</td>
</tr>
<tr>
<td>OARs</td>
<td>Parotid_R</td>
<td>Lung_L</td>
<td>Lung_R</td>
<td>Kidney_L</td>
<td>Kidney_R</td>
<td>Breast_L</td>
<td>Breast_R</td>
<td>heart</td>
</tr>
<tr>
<td>( D_{mean}/D_{max} )</td>
<td>25.44 ± 5.75/29.98</td>
<td>5.36 ± 1.96/22.53</td>
<td>5.26 ± 2.18/14.02</td>
<td>6.94 ± 3.44/15.48</td>
<td>7.41 ± 3.68/16.78</td>
<td>25.15 ± 5.08/30.27</td>
<td>25.92 ± 4.20/30.27</td>
<td>5.66 ± 3.26/14.81</td>
</tr>
<tr>
<td>OARs</td>
<td>Liver</td>
<td>Stomach</td>
<td>Cavity_Oral</td>
<td>Pituitary</td>
<td>Len_L_PRV03</td>
<td>Len_R_PRV03</td>
<td>OpticNrv_L</td>
<td>OpticNrv_R</td>
</tr>
<tr>
<td>( D_{mean}/D_{max} )</td>
<td>6.16 ± 5.65/29.97</td>
<td>3.46 ± 0.55/9.48</td>
<td>11.42 ± 8.92/30.18</td>
<td>3.51 ± 0.56/4.63</td>
<td>6.07 ± 1.10/8.67</td>
<td>6.18 ± 1.25/8.68</td>
<td>10.06 ± 6.36/22.66</td>
<td>8.38 ± 4.95/20.32</td>
</tr>
<tr>
<td>OARs</td>
<td>OpticChiasm</td>
<td>Brainstem</td>
<td>Bowel_Small</td>
<td>SpinalCord</td>
<td>External_Up</td>
<td>External_Down</td>
<td></td>
<td></td>
</tr>
<tr>
<td>( D_{mean}/D_{max} )</td>
<td>2.40 ± 0.23/3.02</td>
<td>2.13 ± 0.13/2.73</td>
<td>7.03 ± 6.35/30.57</td>
<td>3.69 ± 0.56/6.21</td>
<td>15.25 ± 9.09/30.96</td>
<td>14.26 ± 10.42/28.51</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The dose results of bone marrow were that the mean dose of bone_leg, bone_H&N, bone_pelvic, bone_spinal, bone_rib, bone_arm, bone_femer were 5.99 ± 4.68 Gy, 18.03 ± 9.58 Gy, 6.84 ± 6.41 Gy, 3.46 ± 1.46 Gy, 9.52 ± 8.77 Gy, 21.16 ± 5.68 Gy, 3.57 ± 0.43 Gy, respectively (Table 2). The dose results of parallel OARs were that the mean dose of left and right parotid, left and right lungs, left and right kidneys, left and right breast, heart, liver, stomach, cavity oral, pituitary were 25.07 ± 5.81 Gy and 25.44 ± 5.75 Gy, 5.36 ± 1.96 Gy and 5.26 ± 2.18 Gy, 6.94 ± 3.44 Gy and 7.41 ± 3.68 Gy, 25.15 ± 5.08 Gy and 25.92 ± 4.20 Gy, 5.66 ± 3.26 Gy, 6.16 ± 5.65 Gy, 3.46 ± 0.55 Gy, 11.42 ± 8.92 Gy, 3.51 ± 0.56 Gy (Table 2). The dose results of serial OARs were that the max dose of left and right len PRV03, left and right optic nerve, optic chiasm, brainstem, bowel small, spinal...
cord were 8.67Gy and 8.68Gy, 22.66Gy and 20.32Gy, 3.02Gy, 2.73Gy, 2.73Gy, 6.21Gy (Table 2). Overall the dose of total body bone marrow gradually increased as the decreasing distance from the skin, and the doses of OARs were all within the clinically acceptable tolerance.

**Point dose verification**

Tomotherapy cheese phantom was employed for the point dose verification. The point dose deviation was calculated using the formula: deviation = (Dm-Dc)/Dc*100%, where Dm and Dc are the measured dose and calculated dose, respectively. The deviation value is closer to 1 meaning better accuracy, and the deviation of point dose is less than 3%[18][19]. The measurement results (Table 3) showed that the deviations are all within 1%, which met the clinical requirements.

<table>
<thead>
<tr>
<th>Site/Result</th>
<th>Calculate(Gy)</th>
<th>Measure(Gy)</th>
<th>Deviation(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper_Head</td>
<td>1.076</td>
<td>1.081</td>
<td>0.465%</td>
</tr>
<tr>
<td>Upper_Thorax</td>
<td>1.109</td>
<td>1.116</td>
<td>0.631%</td>
</tr>
<tr>
<td>Upper_Abdomen</td>
<td>1.121</td>
<td>1.129</td>
<td>0.714%</td>
</tr>
<tr>
<td>Lower</td>
<td>1.089</td>
<td>1.095</td>
<td>0.551%</td>
</tr>
</tbody>
</table>

**3D Plane Dose Verification**

ArcCHECK was employed for the 3D plane dose verification of the upper and lower segment target. The gamma passing rates (TG119[18] gamma criteria: 3%/3mm, 10% threshold; TG218[19] gamma criteria: 3%/2mm, 10% threshold) were at least 95% and 90%, respectively. The verification results (Table 4) showed that the passing rate was more than 90%, which met the clinical requirements.

<table>
<thead>
<tr>
<th>Site/Result</th>
<th>Passing rate(3%/3mm)</th>
<th>Passing rate(3%/2mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper_Head</td>
<td>96.3</td>
<td>91.8</td>
</tr>
<tr>
<td>Upper_Thorax</td>
<td>95.8</td>
<td>91.3</td>
</tr>
<tr>
<td>Upper_Abdomen</td>
<td>95.1</td>
<td>90.2</td>
</tr>
<tr>
<td>Lower</td>
<td>96.9</td>
<td>91.9</td>
</tr>
</tbody>
</table>

**Multipoint Film Verification**

The film was used for measurement to get multiple point doses, which is also one of the gold standards for dose measurements with TSHT[20][21]. The whole film of Gafchromic EBT3(ISP Corporation, Wayne, NJ, USA) was divided into many small films with a size of 4cm × 5cm. The film was placed in the corresponding simulated position (Fig. 2A) to get the actual point dose (Fig. 2B). The patient carried the split film and wore the 3D printing TPU suit during treatment. The film measurement results (Table 5) showed that most of the measurement results were within 3%, while the regional deviation of excessive motion range was within 5% (such as double nipples, navel, pubic symphysis, etc.), which met the clinical requirements.
Table 5
Statistical result of multipoint film verification

<table>
<thead>
<tr>
<th>Site/Result</th>
<th>Calculate(Gy)</th>
<th>Measure(Gy)</th>
<th>Deviation(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A1</td>
<td>109.11</td>
<td>110.05</td>
<td>0.86</td>
</tr>
<tr>
<td>A2</td>
<td>111.05</td>
<td>112.43</td>
<td>1.24</td>
</tr>
<tr>
<td>A3</td>
<td>106.55</td>
<td>109.71</td>
<td>2.97</td>
</tr>
<tr>
<td>A4</td>
<td>113.95</td>
<td>115.39</td>
<td>1.26</td>
</tr>
<tr>
<td>B1</td>
<td>111.08</td>
<td>115.18</td>
<td>3.69</td>
</tr>
<tr>
<td>B2</td>
<td>112.85</td>
<td>116.82</td>
<td>3.52</td>
</tr>
<tr>
<td>B3</td>
<td>108.65</td>
<td>111.99</td>
<td>3.07</td>
</tr>
<tr>
<td>B4</td>
<td>112.50</td>
<td>108.91</td>
<td>-3.19</td>
</tr>
<tr>
<td>B5</td>
<td>109.85</td>
<td>112.80</td>
<td>2.69</td>
</tr>
<tr>
<td>C1</td>
<td>110.25</td>
<td>113.60</td>
<td>3.04</td>
</tr>
<tr>
<td>C2</td>
<td>114.15</td>
<td>117.99</td>
<td>3.36</td>
</tr>
<tr>
<td>C3</td>
<td>104.25</td>
<td>101.11</td>
<td>-3.01</td>
</tr>
<tr>
<td>C4</td>
<td>111.45</td>
<td>114.80</td>
<td>3.01</td>
</tr>
<tr>
<td>D1</td>
<td>108.15</td>
<td>110.86</td>
<td>2.51</td>
</tr>
<tr>
<td>D2</td>
<td>102.10</td>
<td>106.93</td>
<td>4.73</td>
</tr>
<tr>
<td>D3</td>
<td>113.10</td>
<td>110.80</td>
<td>-2.03</td>
</tr>
<tr>
<td>D4</td>
<td>103.50</td>
<td>108.45</td>
<td>4.78</td>
</tr>
<tr>
<td>E1</td>
<td>107.45</td>
<td>109.56</td>
<td>1.96</td>
</tr>
<tr>
<td>E2</td>
<td>108.53</td>
<td>110.06</td>
<td>1.41</td>
</tr>
<tr>
<td>E3</td>
<td>111.10</td>
<td>113.52</td>
<td>2.18</td>
</tr>
<tr>
<td>E4</td>
<td>112.75</td>
<td>115.25</td>
<td>2.22</td>
</tr>
<tr>
<td>F1</td>
<td>109.35</td>
<td>110.99</td>
<td>1.50</td>
</tr>
<tr>
<td>F2</td>
<td>108.25</td>
<td>110.24</td>
<td>1.84</td>
</tr>
<tr>
<td>F3</td>
<td>110.35</td>
<td>113.99</td>
<td>3.30</td>
</tr>
<tr>
<td>F4</td>
<td>112.25</td>
<td>115.24</td>
<td>2.66</td>
</tr>
</tbody>
</table>

Treatment

MVCT was performed to ensure setup accuracy before each treatment. The maximum setup tolerance was less than 5 mm in three dimensions, and the maximum axial rotation tolerance was less than 1 degree. Considering the upper segment target was relatively long, we used the average correction of the third neck vertebra and the fifth waist vertebra to setup and treat. If the average deviation was greater than 5 mm, the patient should be re-positioned; The lower segment target was scanned near the patella, when the deviation was greater than 5 mm, the position also should be repositioned; while the deviation was less than 5 mm, it was directly corrected. First the patient underwent the upper segment treatment and then the table rotated 180 degrees to make the patient receive the lower segment treatment (Fig. 3). The beam-on time of the upper target was 1519.3 s, the beam-on time of the lower target was 637.7 s, and the total beam-on time was 2157 s (Table 6).

Table 6
beam-on time

<table>
<thead>
<tr>
<th>Site</th>
<th>Beam-on time(s)</th>
<th>Total beam-on time(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper</td>
<td>1519.3</td>
<td>2157.0</td>
</tr>
<tr>
<td>Lower</td>
<td>637.7</td>
<td></td>
</tr>
</tbody>
</table>

Radiation Toxicity
To ensure the safety of the elder patient, hematology tests were performed during the treatment period, such as routine blood, complete biochemical tests, erythrocyte sedimentation rate, coagulation, and the routine imaging such as B-ultrasound, CT, PET-CT. After 12 fractions, the radiotherapy was terminated due to fatigue, nausea, vomiting, low-grade fever. The platelet count dropped to 50 x 10^9/L, the white blood cells dropped to 2.0 x 10^9/L, and degree bone marrow suppression occurred. The treatment was terminated by the physician considering the patient's older age and treatment safety. Recombinant human granulocyte stimulating factor and recombinant human thrombopoietin were examined, the adverse hematomal reaction was improved, and it returned to the clinically normal range after one week of continuous recovery.

Discussion

The traditional treatment of MF usually uses TSEI[3], the dual-frame six-field irradiation technology developed by the Stanford University School of Medicine was widely used[4], but there are many disadvantages, such as poor dose distribution and homogeneity, poor comfort and setup reproducibility, long treatment time, etc.[4]. HT can achieve ultra-long target treatment (160cm x 40cm) and dose-printing distribution, which is very suitable for the long and complex targets, such as total body multiple metastatic irradiations, craniospinal irradiation, total body irradiation, total marrow irradiation, etc.[6]. Hsieh CH et al.[7] first used HT to achieve TSHT; Schaff EM et al.[17] and Sarfehnia A et al.[22] also used HT to perform total skin irradiation, these studies showed the advantages of TSHT.

So far there is no report about TSHT of MF using total skin bolus by 3D printing technology. Based on our previous experience with TSHT where six patients using diving suits had been treated before, we studied the patient during the whole process of TSHT treatment[14]. A customized 3D printed TPU suit was used as a bolus, which solved the problem of insufficient skin dose deposition. It achieved uniform dose distribution, good fitness, a simple implementation process, good treatment effect, and low toxicity effects, it will provide one more treatment method and better clinical effects for the treatment of MF.

In this work, a 5mm TPU suit by 3D printing was used as a bolus to increase the skin dose. Hsieh CH et al.[7] used a 3mm diving suit as a bolus to make 90% of the target reach the prescribed dose. Schaff EM et al.[17] investigated two patients with MF to confirm that TSHT can substitute traditional TSEI using a 3mm diving suit as a bolus, the film verification proved that a diving suit can significantly increase the skin dose. Deveau MA et al.[8] treated a dog with cutaneous epitheliotropic lymphoma and 3D printing technology was used to produce a 10mm thick 3D mold scaffold with a density of 1.09g/cm^3, achieving 92% of the target to reach the prescription dose. Baltz GC et al.[9] used 3D printing technology to produce whole scalp bolus to achieve total scalp irradiation treatment. So far there is no report about TSHT of MF using total skin bolus by 3D printing technology.

The prescription dose is 24 Gy in 24 fractions, and 5 times per week. The field width, the modulation, the pitch, and the dose grid are 5cm, 3, 0.287, and 0.195cm x 0.195cm, respectively. The key factor is the complete block with the distance to PTV that has a significant influence on the plan quality, this patient used a 4cm distance consistent with the results of previous studies[14].

Compared with the lower target, the dose distribution of the upper target is slightly worse, and the CI and HI index are consistent, the main reason is that the left and right arms make the lateral width greater than 40 cm, causing blind areas in certain angles unable to be irradiated. Sarfehnia A et al.[22] also had an overdose or underdose for the left and right arm during the TSHT of a child. How to deal with the right and left arm doses needs further research.

The most radiation toxicity is bone marrow suppression in the previous literature research. Schaff EM et al.[17] used TSHT in 12 Gy with 8 fractions, the mean dose of total bone marrow was controlled to 1.66 Gy, and finally grade bone marrow suppression occurred. Hsieh CH et al. [7] had similar bone marrow suppression rates used TSHT at a higher prescribed dose of 30 Gy. Why the patients experienced severe bone marrow suppression with such a low bone marrow dose, one explanation is that the TPS may not accurately simulate the actual bone marrow dose, another explanation is that the plan parameter with the mean bone marrow dose less than 2 Gy is not strict or predictable for the TSHT. To avoid the toxicity, total bone marrow was outlined one by one, such as bone_leg, bone_H&N, bone_pelvic, bone_spinal, boneRib, bone_arm, bone_femur, strict dose limitations for bone marrow in plan design to reduce dose. The bone marrow dose has obvious differences as the closer distance to the skin. The bone_H&N, bone_femur, etc. are farther from the skin than bone_pelvis, bone_spinal, etc., so they relatively received slightly lower dose. Whether to reduce the bone marrow dose to lose part of the target or to increase the bone marrow dose to ensure the target prescribed dose needs to be determined by the physician based on the patient's situation. Although the 3D printed TPU suit as a bolus can increase the skin dose deposition, the patient is thin and part of the bone marrow is close to the skin, it was difficult to reduce enough conditions, which caused degree bone marrow suppression occurred when the patient was irradiated to the 12th, and the treatment was terminated.

MF is usually highly radiosensitive. Radiotherapy plays a major role in the treatment of MF and is also one of the recommended treatment methods[23]. The prescribed dose can be selected from a wide range according to the purpose of the treatment, normally 15–20 Gy is sufficient for palliative treatment, but recent studies showed that the complete remission rate is only 55% for 10–20 Gy, when the dose reaches 30 Gy or
more, the complete remission rate can reach 94%, the dose of a single course of treatment should generally not exceed 36 Gy, otherwise, the acute phase response will be severe[2]. The recommended prescription dose of cutaneous lymphoma from the European Organization for Research and Treatment of Cancer (EORTC) consensus is 30-36 Gy during 6-10 weeks, and should be reached at least 26 Gy in a cone-shaped skin at a depth of 4 mm along the central axis[23]. However, the low-dose model has been gradually promoted in recent years, and the main feature is the shorter treatment time and the lower toxicity effects. The prescribed dose selected in this study is 24 Gy with 24 fractions, 5 times per week. The choices of different research institutes are not completely consistent. Hsieh CH et al.[7] used a 30 Gy with 40 fractions. Schaff EM et al.[17] used a 12 Gy with 8 fractions; Haraldsson A et al.[21] used a 32 Gy with 24 fractions. Therefore, different institutes need to choose an appropriate prescription dose and the number of fractions according to the actual situation of the patient.

The measured dose was not much different from the calculated dose, which is consistent with the results by Akbas U et al.[25]. The D2 and D4 deviations were more than 3% due to bolus fit and involuntary movements, but both were less than 5%. B4, C3 and D3 deviations are lower because of the fit of the bolus and involuntary slight movement. For the B3, B5, C2, C4, D2 and D4 on the left and right arms, since the degree of freedom of the arm was larger than the body and the repeatability was poor, resulting in the regional deviation as slightly larger the total body from the shoulder to the palm, but they were all within 3%. On the hand, the deviation was due to segmented treatment, the measured films received the scattered rays during the treatment of other segments. On the other hand, the inaccurate calculation of the surface dose by the planning system may also cause the dose deviation[26], measured films also receive the extra dose by MVCT, which was also a factor that the deviation to be slightly higher. In general, most of the results were within 3%, and even the regional deviation of excessive motion range was within 5%, which ensured the accuracy of the delivered dose.

The beam-on time of the upper target was 1519.3 s, the beam-on time of the lower target was 637.7 s, and the total beam-on time was 2157 s (Table 6), which was about 25.3 min. The customized TPU suit is not as convenient as a conventional diving suit, which need to be worn in the treatment room and requires an additional half hour. The preparation time, the setup time and the MVCT image guide were added up to one and a half hours. Compared with the two and a half hours of TSEI, the time has been shortened by nearly half[27], which has significantly improved the treatment efficiency. The patient was more comfortable and maintains the repeatability of the position well in the supine position than in the traditional standing treatment. At the same time, the intensity-modulated treatment plan has greatly improved the HI and CI, thus ensuring the accuracy and safety of the treatment.

The deviation for TSEI between the measured dose and calculated dose can reach up to 40%, such as the perineum and eyelids can be as high as 90%[25]. In addition, the depth of skin tumors was usually more than 4 mm, so there was an insufficient dose by TSEI. HT has advantages in long target, which provides uniform dose, precise dose depth control and low organ toxicity[26] and TSHT can be used instead of TSEI. In this case, the upper and lower target reached 95% of the prescribed dose, and the maximum dose was 115%. The dose deviation was much smaller than TSEI. At the same time, the complete block was 4 cm away from PTV significantly reducing the internal OARs dose, which greatly decreased the incidence of toxicity.

**Conclusion**

The total skin bolus by 3D printing was first used to treat MF with TSHT, 3D printing technology shows its advantages: flexibility, fitness, etc. but there were still disadvantages: skin gaps, wearing inconvenience, etc. Therefore, there are still many aspects for improvement in the 3D printed suit which is also the direction of future research.

**Materials And Methods**

**Patient Selection**

The patient is a 65-year-old female with a 3-year history of MF, which was admitted to the department of radiation oncology of the First Affiliated Hospital of Zhengzhou University in June 2021 for pre-TSHT. The clinical diagnosis stage is T₄N₀₋₂M₀B₀.

**Bolus**

Before the patient underwent TSHT, the total body computed tomography (CT) had been scanned and imported to Mimics17 software with digital imaging and communications in medicine (DICOM) format, and the patient's external contour was reconstructed and output in STereoLithography (STL) format for 3D printing. To improve the flexibility and simulation of the bolus, a flexible printing material with certain elasticity named TPU is selected for printing with a thickness of 5 mm and a CT value of about 200 HU. Since the 3D printer can only achieve a maximum range of 30 x 30 x 30 cm³, multiple segmentations are spliced to form a completed total skin bolus for the patient. As Fig. 4A shows, the patient dressed the 5 mm TPU as bolus and the bolus was tailored according to patient's external-external shape in order to be easier to put on and take off.
Immobilization

The patient wearing a 5 mm TPU suit was immobilized in a supine position (Fig. 4B). Thermoplastic masks were used for the head, neck, thorax, and abdomen, while lower limbs were immobilized in a vacuum cushion.

Image Acquisition At Simulation

CT scans (SOMATOM Definition AS40, Siemens) were performed under the following condition: a scan and reconstruction slice thickness of 5 mm. The patients were scanned in the upper and lower segment, the segment line made of lead was located around 10 cm above the patella, while the upper marks and lower masks were located near the patient's belly button and the patient's patella, respectively. The upper segments were scanned from the skull to 10 cm below the boundary while the lower segment was from the toes to 10 cm above the boundary (Fig. 5).

Delineation Of Target Volumes And Organs At Risks (Oars)

The two sets of CT images were transferred to the physician's workstation (Eclipse 13.5; Varian, Palo Alto, CA, USA) for delineation. The target volumes and OARs were delineated by radiation oncologists based on the planning CT according to the ICRU50[10] and ICRU62[11]. The clinical target volume (CTV) was defined between the skin surface and 5 mm below it[7]. The planning target volume (PTV) was generated by expanding the CTV by 5 mm and then retracting it by 3 mm in the outside region considering the setup error and dose built-up effect. OARs were delineated based on the ICRU 83 report[12], primarily including the total bone marrow (bone_leg, bone_H&N, bone_pelvic, bone_spinal, bone_rib, bone_arm, etc.), parotid, lung, kidney, breast, heart, liver, etc. The junction between the upper and lower segment of total body irradiation (TBI) has been studied in our previous publication and the dose in the overlap region was mostly homogeneous when the distance was equal to the FW[13].

Plan Designs

The planning CT and contoured structures of the patient were transferred to the treatment planning workstation (Version 5.1.6; Accuray, Sunnyvale, CA, USA) for planning. The prescription dose is 24 Gy in 24 fractions, and 5 times per week. The remaining center volume was set to complete mode after 4 cm away from the PTV[14], which was used as an auxiliary structure for plan optimization to achieve dose control. Two plans were designed for the upper and lower target, correspondingly. The field width, the modulation, the pitch, and the dose grid were 5 cm, 3, 0.287, and 0.195 cm × 0.195 cm, respectively.

Evaluation Of Plan Quality

The parameters evaluated for the patients included the mean dose, the heterogeneity index (HI) and the conformity index (CI) of the target volume. At least 95% of the target volumes reached the prescribed dose. The HI was calculated using the formula, $HI = \frac{D_{5\%}}{D_{95\%}}$, where $D_{5\%}$ and $D_{95\%}$ are the dose received by 5% and 95% of the PTV volume. The HI value greater than 1 represents the heterogeneity dose distribution of the target volume. The CI was obtained using the following Paddick equation[15], $CI = \frac{V_{T,ref}}{V_T} \times \frac{V_T}{V_{ref}}$, where $V_{T,ref}$ is the target volume covered by the prescription isodose (cm$^3$), $V_{ref}$ is the volume covered by the prescription isodose (cm$^3$), $V_T$ is the target volume (cm$^3$). The closer CI value to 1, the better dose conformity of the target volume. Strict requirements were implemented for the dose of OARs as the maximum dose of the lens plan risk volume (PRV), the mean dose to the lung, the mean dose to the left and right kidneys, and the mean dose to the liver are less than 9 Gy, 8 Gy, 7 Gy, and 8 Gy[16], respectively. Bone marrow is very sensitive to radiation, it was considered as the most important OARs for treatment. It has been confirmed that the total dose of bone marrow irradiation is related to blood toxicity, especially the side effects of bone marrow suppression in the skull, while the mean dose of ribs and sternum were minimized under the premise of safety[17].

Dose Verification

Three kinds of dose verification techniques were performed, including point dose verification with Cheese Phantom, 3D plane dose with ArcCHECK and total body multi-point film verification with US Gafchromic EBT3 film. The gamma analysis criteria referred to TG119[18] and TG218[19]. The gamma passing rates for criteria of 3%/3 mm and 3%/2 mm were above 95% and 90% respectively, while the deviation of point dose was less than 3%.

Treatment
Image guidance radiotherapy (IGRT) was performed for every treatment. Considering the upper segment target was relatively long, we used the average correction of the neck and waist for setup and treatment. For the lower segment target, the correction of the patella is used for setup and treatment.

**Clinical Observation**

To ensure the safety of the elder patient, hematology tests were performed during the treatments, including routine blood test per two days, complete biochemical tests, erythrocyte sedimentation rate, coagulation test per week, and routine imaging including B-ultrasound, CT, or PET-CT. After 10 fractions, the blood indicators began to decline. After 12 fractions, the radiotherapy was terminated due to fatigue, nausea, vomiting, low-grade fever, and degree bone marrow suppression.

**Declarations**

**Ethics approval and consent to participate**

The study was approved by the Clinical Research Ethics Committee of Zhengzhou University. 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 World Medical Association Declaration of Helsinki (version 2002) and the additional requirements. All patients signed informed consent.

**Consent for publication**

All authors approved the final manuscript and the submission to this journal.

**Availability of data and materials**

Written informed consent was obtained from the individual for the publication of any potentially identifiable images or data included in this article. The data are not publicly available due to privacy or ethical restrictions.

**Competing interests**

Author XP was employed by Anhui Wisdom Technology Co. The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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**Authors’ contributions**

Paper idea: HW, YP, CL, XW, YG, LL, XP, and XX. The source of datasets: HW, YP, CL, XW, LL, and XP. Writing of the paper: HW, YP, CL, XW, YG, XP, XX. 3D Printing: LL, All authors contributed to the article and approved the submitted version.

**References**


**Figures**

**Figure 1**

The dose distribution of the upper and lower segment target in the *transverse*, coronal and sagittal plane
Figure 2

Schematic diagram of simulated and measurement points for film verification

Figure 3

Patients are treated in upper and lower segment
Figure 4

The patient wearing the TPU suit and position of immobilization
Figure 5

The patients scanning in the upper and lower segment target