Biologically corrected display of isodoses in radiation treatment plans in Eclipse 15.6 – Development of a prototype using ESAPI script

E. Blank^{1,2)}, C. Schröder⁴⁾, M. Grohmann⁵⁾, M. Krüger^{1,2)}, S. Kirschke^{1,2)}, P. Grundmann^{1,2)}, C. Bergmann^{1,2)}, R. Wiener^{1,3)}, O. Stoiber^{1,2)}, A. Buchali^{1,2)}

- 1) Ostprignitz-Ruppiner Gesundheitsdienste GmbH, Neuruppin, Germany
- ²⁾ Medizinische Hochschule Brandenburg, Neuruppin, Germany
- 3) Beuth Hochschule für Technik Berlin, Fachbereich II, Berlin, Germany
- ⁴⁾ Institut für Radioonkologie, Kantonsspital Winterthur, Winterthur, Swizerland
- ⁵⁾ Universitätsklinikum Hamburg Eppendorf, Germany

Corresponding Author:

Dr. rer. nat. Eyck Blank
Ostprignitz-Ruppiner Gesundheitsdienste GmbH
Fehrbelliner Strasse 38
16816 Neuruppin
Germany
e.blank@ruppiner-kliniken.de

Abstract

Background: In radiation oncology, different fractionation schemes can be compared converting the actual dose into the equivalent dose in 2 Gy fractions (EQD2). The focus of the current project was to create an ESAPI script (Eclipse Scripting API) for this kind of biological dose correction of the 3D dose matrix displayed in the radiation treatment planning system Eclipse (Aria, Varian Medical Systems, A SIEMENS Healthineers Company). Thereby, the goal was to make the biological dose correction topologically visible by conversion of the entire 3D dose distribution, thereby providing an additional tool for plan evaluation.

Results: In C#, a script for the biological dose correction of the 3D dose matrix was generated ("EB Bio3D"). The script was implemented and successfully tested using real life patient cases.

Conclusion: The above mentioned software was developed and implemented. Tests were performed on several patient plans and confirm the correct functioning of the ESAPI script *EB_Bio3D*. A clinical test run will be started.

Keywords: radiation therapy, treatment planning, software, equivalent dose

Background

In radiation oncology, the biological effect of the radiation both on the target volume and the organs at risk depends on the dose delivered per fraction. This can by described using the linear-quadratic model [5]. In clinical practice, the equivalent dose in 2 Gy fractions (EQD2) is used to normalize any given fraction dose to a fraction dose of 2 Gy, therefore enabling the comparison of different dose schemes. The focus of this project was to create an ESAPI script (Eclipse Scripting API) for biological dose correction of the 3D dose matrix. Although a solution for manipulating dose matrices for nuclear medicine applications [2] has already been published along with code basics in Python [1], it was not clear if this project could be solved in C# with Eclipse 15.6. Given that the ESAPI libraries for Python and ESAPI are the same [Keranen] and there is an online description of ESAPI [3] the current project was initiated. The idea of this was based on a published Python script for biological conversion of gynecological brachytherapy plans [12].

The focus of this work is the technical aspect of data conversion and display using the above mentioned script. Data on biological correction of dose values [8,10,11] in DVH curves has been published before [9]. The biological correction of DVH curves is mathematically simple, since an organ-specific separation of the dose values is already available and they are already statistically compressed. Due to the monotonic, quasilinear behavior of the linear-quadratic conversion, a reduction of the problem to the DVH conversion is valid [9].

The goal of this project is to make the biological dose correction topologically visible by conversion of the entire 3D dose distribution, thereby providing an additional tool for plan evaluation. This conversion can be of great importance in the planning of re-irradiations. While the use of voxel-based EQD2 (Equivalent Dose 2Gy/Fx) conversion for re-irradiation has been demonstrated with other systems [13,14,15], implementation using ESAPI would be a first.

Debugging support as well as configuration parameter offloading was be realized through Excel.

Implementation

Workflow

With an in-house ESAPI script *EB_Bio3D*, a verification plan without radiation fields, which incorporates the biologically corrected EQD2 dose distribution as an *EvaluationDose*-Matrix, is generated from an radiation treatment plan. The detour via a verification plan is necessary since dose matrices in calculated radiation treatment plans are not editable to ensure that unintentional misinterpretations cannot occur.

The main problems of this script are the following:

- 1. Creation of a verification plan with an EvaluationDose-Matrix
- 2. Conversion of the original dose distribution stored in *RawValue* into an absolute fractional dose distribution
- 3. Separation of dose points to individual organ structures
- 4. Organ-specific biological dose correction according to EQD2
- 5. Reconversion of the EQD2 dose distribution into RawValues to be stored back in Eclipse
- 6. Creation of an in-house code debugging tool using Excel
- 7. Excel file to store all necessary configuration parameters

Tests of this ESAPI script will be performed on various irradiation schedules.

Data import

The advantage of user-specific software based on ESAPI is the practicable handling in Eclipse. Without prior export and import, planning data can be retrieved directly from Eclipse for external processing by means of context-related libraries.

The code for context-related link to the required planning data can be found in fig. 1.

```
184 // patient and plan context
185 Patient Pat = context.Patient;
186 PatLName = context.Patient.LastName.ToString();
187 PatFName = context.Patient.FirstName.ToString();
188 PatID = context.Patient.Id.ToString();
189
190 context.Patient.BeginModifications();
191
192 Course eCourse = context.Course;
193
194 ExternalPlanSetup plan = context.ExternalPlanSetup;
195
196 if (context.Patient == null || context.StructureSet == null)
197 {
198
       MessageBox.Show("Please load a patient, 3D image, and structure
       set before running this script.", SCRIPT NAME, MessageBoxButton.OKCancel,
       MessageBoxImage.Exclamation);
199
       return;
200 }
```

Fig. 1: Context-related data import (lines 185-194)

The first problem to consider is the interception of the different notations of the structure IDs needed for biological conversion. The use of clinical templates in treatment planning does not guarantee a standardized ID notation, making hard coded structure management error-prone. Goss tumor volume (GTV) IDs, which contain labels for treatment dose as well as anatomical location, are particularly problematic in this regard. For GTV this was solved by reading the structure list beforehand (*fig. 2*). The individual GTV in the structure list are identified by substring analysis.

```
201 StructureSet ss = context.StructureSet;
203 foreach (Structure s in ss.Structures)
204 {
       if (s.Id.Length>3)
206
              if (s.Id == BODY ID1 | s.Id == BODY ID2) // because
2.07
              upper-/lowercase
208
209
                      sBody = s.Id;
210
211
              if (s.Id.Substring(0,3) == "GTV")
212
213
                      gtv.Add(s.Id);
                      gtvls.Add(s);
215
216
217 }
```

Fig. 2: Reading the GTV as structure list (lines 201-217) and substring analyse (line 211)

Another problem to consider during biological conversion are overlapping structures. Although individual organ structures are mutually exclusive, GTV structures may overlap individual organ structures with different radiobiological behavior. GTV are usually considered to have higher α/β values because of their poorer repair properties. The expansion to generate the planning target volume (PTV) are not considered in the enlarged α/β values, because here it is assumed that these behave like healthy tissue. In code terms, the dominance of the GTV during conversion is realized by placing them at the end of the processing chain (*fig. 3*). The conversion is carried out twice in the overlapping areas, which leads to longer computing times. However, this was accepted for this ESAPI prototype.

```
421 if (dose != null)
422 {
423
         for (int zi = 0; zi < dose.ZSize; zi++)</pre>
424
425
                 zm[zi] = zi * dresZ + doZ;
426
                 dose.GetVoxels(zi, zbuffer);
                                                      // here read a dose layer
427
428
                 dbi[zi] = zbuffer[90, 54];
                                                      // only for test by debuging,
                                                              how look the dose values
429
430
                 for (int yi = 0; yi < dose.YSize; yi++)</pre>
431
432
                          ym[yi] = yi * dresY + doY;
433
434
                           for (int xi = 0; xi < dose.XSize; xi++)</pre>
435
436
                                    xm[xi] = xi * dresX + doX; // calculate carthesian
                                                                       points of matrix points
                                                                        for PointInsideSegment
437
438
                                    VV[1] = ym[yi];
                                    VV[2] = zm[zi];
439
440
441
                                    // IsPointInsideSegment for all entities
443
                                    // EQD2 conversion by a/b values
445
                                    // imageMatrix und doseMatrix have different
446
                                    // IsPointInsideSegment must have carthesian coordinates
447
                                    // x, y, z must converted by Xres, Yres, Zres and Origin
448
449
                                    dbuffer[xi, yi] = dose.VoxelToDoseValue(zbuffer[xi, yi]).Dose * GD / 100;
450
                                    ebuffer[xi, yi] = 0;
451
452
                                    // Body
453
                                    if (body.IsPointInsideSegment(VV))
454
455
                                             if (body != null)
456
                                                     ebuffer[xi, yi] = (dbuffer[xi, yi]/Frakt +
          abBody) / (2 + abBody) * dbuffer[xi, yi];
457
458
459
460
461
                                    // Hirn (brain)
462
                                    if (hirn != null)
463
464
                                             if (hirn.IsPointInsideSegment(VV))
465
                                                     466
468
469
748
                                    // GTV list (gtvls)
749
                                    if (gtvls != null)
750
751
                                             foreach (Structure s1 in gtvls)
752
753
                                                      if (s1.IsPointInsideSegment(VV))
754
                                                               ebuffer[xi, yi] = (dbuffer[xi, yi]/Frakt
+ abGtv) / (2 + abGtv) * dbuffer[xi, yi];
756
759
```

Fig. 3: End placement of GTV list (lines 749-758) in EQD2 conversation chain (lines 452-758)

2.3 Conversion

Biological dose conversion is performed using the linear quadratic model proposed by Lyman et al [3,4,5,6,7]. The values are organ-specific, which is why a structure query is necessary (fig. 4).

```
721 // Darm (bowel / gut)
722 if (darm != null)
723 {
724
        if (darm.IsPointInsideSegment(VV))
725
                 ebuffer[xi, yi] = (dbuffer[xi, yi]/Frakt + abDarm) / (2 + abDarm) * dbuffer[xi, yi];
726
727
728 }
729
730 // Rektum (rectum)
731 if (rektum != null)
732 {
733
        if (rektum.IsPointInsideSegment(VV))
734
735
                 ebuffer[xi, yi] = (dbuffer[xi, yi]/Frakt + abRektum) / (2 + abRektum) * dbuffer[xi, yi];
736
737 }
738
739 // Blase (bladder)
740 if (blase != null)
741 {
742
        if (blase.IsPointInsideSegment(VV))
743
744
                  ebuffer[xi, yi] = (dbuffer[xi, yi]/Frakt + abBlase) / (2 + abBlase) * dbuffer[xi, yi];
745
746 }
```

Fig. 4: Organ-specific EQD2 conversion (lines 726, 735, 744) and structure query (lines 724, 733, 742)

Before the conversion can be performed, it is necessary to consider how the dose matrix is stored in the Eclipse plan. It should be noted that the dose values in the matrix are stored as relative *RawValue*. These must be converted into absolute fractional dose values beforehand (*fig. 5*).

The assignment of the dose points to the individual structures works with Cartesian point coordinates. For this purpose, a conversion of the matrix indices into Cartesian point coordinates (vector v[,,]) is necessary (fig. 5).

```
376 var dose = plan.Dose;
386 int dSizeIX = dose.XSize;
387 int dSizeIY = dose.YSize;
388 int dSizeIZ = dose.YSize;
389
390 double doX = dose.Origin.x;
391 double doY = dose.Origin.y;
392 double doZ = dose.Origin.z;
393
394 double dsizeX = dose.XSize;
395 double dsizeY = dose.YSize;
396 double dsizeZ = dose.ZSize;
397
398 double dresX = dose.XRes;
399 double dresY = dose.YRes;
400 double dresZ = dose.ZRes;
402 int[,] zbuffer = new int[dose.XSize, dose.YSize];
403 double[,] dbuffer = new double[dose.XSize, dose.YSize];
404 double[,] ebuffer = new double[dose.XSize, dose.YSize];
408 double[] xm = new double[dose.XSize];
409 double[] ym = new double[dose.YSize];
410 double[] zm = new double[dose.ZSize];
412 EvaluationDose eDose = ePlan.CreateEvaluationDose();
413 ePlan.CopyEvaluationDose(dose); // to fit dimensions of dose matrices dose und eDose !
414 double fraktDose = plan.DosePerFraction.Dose;
415 int fractNumber = (int)plan.NumberOfFractions;
416 DoseValue ee = new DoseValue(fraktDose, DoseValue.DoseUnit.Gy); // prepare fraction dose for new ePlan
417 ePlan.SetPrescription(fractNumber, ee, 1.0); // here set fraction number and fraction dose of ePlan in ARIA
419 // whole 3D matrix will be scanned
420 VVector VV = new VVector(0,0,0);
421 if (dose != null)
423
        for (int zi = 0; zi < dose.ZSize; zi++)</pre>
424
425
        zm[zi] = zi * dresZ + doZ;
        dose.GetVoxels(zi, zbuffer); // here read a dose layer
426
427
428
        dbi[zi] = zbuffer[90, 54]; // only for test by debugging, how look the dose values
429
430
        for (int yi = 0; yi < dose.YSize; yi++)</pre>
431
                 ym[yi] = yi * dresY + doY;
433
                 for (int xi = 0; xi < dose.XSize; xi++)</pre>
435
436
                          xm[xi] = xi * dresX + doX; // calculate carthesian points of matrix points
                                                            for PointInsideSegment
                          VV[0] = xm[xi];
                          VV[1] = ym[yi];
438
439
449
                          dbuffer[xi, yi] = dose.VoxelToDoseValue(zbuffer[xi, yi]).Dose * GD / 100;
                          ebuffer[xi, yi] = 0;
450
```

Fig. 5: Conversion the raw values of dose into fractional dose values (lines 426, 449), Buffer matrices zbuffer[,], dbuffer[,], ebuffer[,] (lines 426, 449, 450), Conversion the matrix indices into Carthesian coordinate vectors needed for structure query of dose points (lines 425, 432, 436-439).

Adjustment of dose matrix to the DICOM Orign (lines 386-400,425,432, 436)

The fractional dose values are used to perform the EQD2 conversion, which is performed iteratively through the entire 3D dose matrix.

To avoid double use of the EQD2 formula, multiple buffer matrices are used. The original relative *RawValue* dose values in *zbuffer[,]* are stored as absolute fractional dose values in *dbuffer[,]*. The EQD2 dose values are ultimately located in *ebuffer[,]* (fig. 5).

Since ESAPI only allows the dose data to be read out layer by layer, the conversion process is also performed layer by layer with two-dimensional buffer matrices *zbuffer[,]*, *dbuffer[,]* and *ebuffer[,]* (*fig.* 6).

```
760
                           // all ebuffer reconvert into relative values
761
                           ebuffer[xi, yi] = ebuffer[xi, yi] * 100 / GD;
762
                           if (ebuffer[xi, yi] < 0)
763
764
765
                                    ebuffer[xi, yi] = 0;
766
767
                           DoseValue eee = new DoseValue(ebuffer[xi, yi], DoseValue.DoseUnit.Percent);
768
769
770
771
                           zbuffer[xi, yi] = (int)eDose.DoseValueToVoxel(eee) ;
772
773
774
775
         // dbu[zi] = ebuffer[90, 54]; // for Excel debugging
         // dbi[zi] = zbuffer[90, 54];
785
         eDose.SetVoxels(zi, zbuffer);
787 }
```

Fig. 6: Back conversion the EQD2-EvaluationDose matrix into RawValues layer by layer (line 761-769) Back writing the converted RawValues into ARIA data base (line 785)

At the end of the conversion process, the EQD2 values must be converted back to raw dose values. This is done with the function *DoseValueToVoxel()*. Since *SetVoxels()* requires the so-called *DoseValue* type as parameter instead of dose values as double, a small additional step of converting double to *DoseValue* is necessary.

Excel Debugger

An important additional help is the possibility to debug the ESAPI code during development time. Since the script works context based, Eclipse must be started each time to test it. In Eclipse, there is no native way to debug as there is under an Integrated Development Environment (IDE). There is the possibility to use a PluginRunner [16,17] to run the script directly from the IDE. However, this requires code intervention. Another possibility is to attach an Excel interface that is often needed in ESAPI scripts anyway (*fig.* 8). This allows variable values to be easily read out for runtime under Eclipse (*fig.* 7).

Fig. 7: Commented Excel-function call, could be inserted everywhere in the code.

The parameter list should be adapted (lines 793-806)

```
813 // Debugging Excel
815 private void UpdateExcel(string S1, string S2, string S3, string S4, string, S5, string S6, string S11, string S12, string S13,
                                           string S100, string S101, string S102, string S103, string S104, string S105,
                                           string S194, string S195, string S196, string S197, string S198, string S199)
829 {
830
              Excel.Application oXL = null;
              Excel._Workbook oWB = null;
Excel._Worksheet oSheet = null;
831
833
              try
835
836
                             oXL = new Microsoft.Office.Interop.Excel.Application();
                            OWB = OXL.Workbooks.Open("Q:/ESAPI/Flugins/EB_Bio3D/EB_Bio3D.xlsx");
OSheet = String.IsNullOrEmpty("Tab1") ? (Microsoft.Office.Interop.Excel._Worksheet)oWB.ActiveSheet:
(Microsoft.Office.Interop.Excel._Worksheet)oWB.Worksheets["Tab1"];
838
840
                            // Excel Sheet Test
841
                            // read the row counter in Excel
                            string sReihe = oSheet.Cells[1, 1].Value == null ? "-" :
oSheet.Cells[1, 1].Value.ToString();
int iReihe = Convert.ToInt32(sReihe);
843
844
                             iReihe = iReihe + 1;
846
847
                             // dresX
                            oSheet.Cells[iReihe, 1] = S1;
oSheet.Cells[iReihe, 2] = S2;
oSheet.Cells[iReihe, 3] = S3;
849
851
                             // doX
                             oSheet.Cells[iReihe, 4] = S4;
                            oSheet.Cells[iReihe, 5] = S5;
oSheet.Cells[iReihe, 6] = S6;
853
854
                            Obsert.Cells[iReihe, 0] = 30,
// dsizeX
Obsert.Cells[iReihe, 8] = S11;
Obsert.Cells[iReihe, 9] = S12;
Obsert.Cells[iReihe, 10] = S13;
856
858
867
                             // curve data
                            oSheet.Cells[10, 4] = S100;
oSheet.Cells[11, 4] = S101;
868
870
                             oSheet.Cells[12, 4] = S102;
974
                             oSheet.Cells[107, 4] = S197;
oSheet.Cells[108, 4] = S198;
                             oSheet.Cells[109, 4] = S199;
978
                             // write bach the row counter in Excel
                             sReihe = Convert.ToString(iReihe);
oSheet.Cells[1, 1] = sReihe;
                             // and save Excel
                             oWB.Save();
983
984
               // Quit after saving Excel
986
              catch (Exception ex)
{
988
                            MessageBox.Show(ex.ToString());
989
990
991
               finally
                            if (oWB != null)
993
                                           oWB.Close(true, null, null);
995
996
997
998
```

Fig. 8: Excel function for reading and writing into an Excel file (lines 768-956)

However, some *using* clauses and *Referencies* are required to include an Excel file interface (*fig. 9*). Furthermore, Excel files can also be used as ini or config files. User-specific script configurations can be easily stored in these files without having to hardcode them.

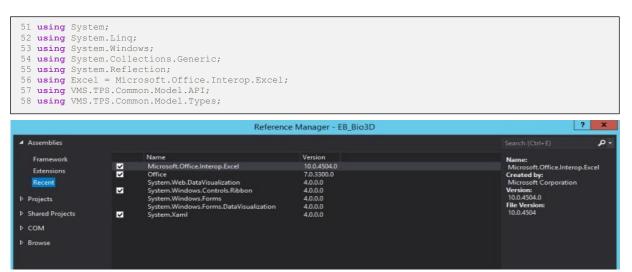


Fig. 9: Using clauses (line 56, upper fig.) and referencies, to embed the Excel Routine into C# Code(lower fig.)

In the broader context Excel files are advisable under ESAPI, because test results can be stored not only for documentation purposes, but can be processed later effortlessly without script. ESAPI thus only becomes necessary as an interface for later external data collection and evaluation.

The EB_Bio3D script will be described in more detail in an ESAPI Cookbook 2021. After publication of the cookbook, the code will also be available on github [18].

Results

Patient example

The function of the script for EQD2 conversion is shown on the following figure as an example of a pelvic irradiation with 60Gy total dose and 2Gy fractional dose (fig. 10).

The original plan is shown on the left and the biologically corrected EQD2 dose distribution on the right. The comparison looks plausible. While in the central GTV area (blue structure line) original and EQD2 dose distribution are almost the same ($\alpha/\beta = 8$), EQD2 is significantly reduced in the rest of the area with an α/β value of 2 and smaller local fractional dose (<2Gy).



Fig. 10 Comparison of original plan (left) and EQD2 converted evaluation plan (right). The red lines mark the comparison profile curves

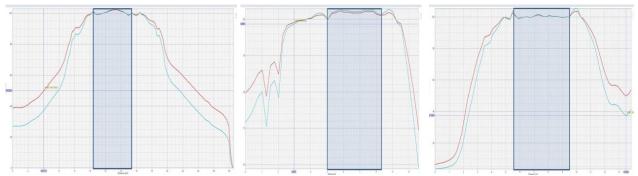


Fig. 11 Dose profile comparison original plan (red) and EQD2 converted evaluation plan (blue) transversal(left), pa-ap (middle), caudal-cranial (right). The blue shaded area marks the profile area lying in the GTV. The jags in the left part of the middle curve are air pockets in the rectum

In *PlanEvaluation*, different profile curves of the original plan and EQD2 plan are compared (*fig. 11*). Plausibility is checked. Attention is paid to the fact that the curves overlap without offset, that there are no dropouts (unconsidered dose points in the EQD2 conversion) and that the organ-specific conversions are confirmed by recalculation.

Testing of the ESAPI Script

The following describes how the script has been checked for correct operation. The first problem of interest is whether the output dose and evaluation dose distributions have no offset from each other. This error possibility is due to the fact that image (structure) matrix and dose matrix in the code have to be adjusted separately and individually with respect to the DICOM Origins (*fig. 5*).

This origin adjustment is significant for the generation of the metric dose point vectors of the dose matrix indices for organ assignment of the individual dose matrix points.

In the profile curve comparison in all three spatial directions, a superposition of the curve structures is seen as expected (fig. 11).

The next test aspect is the detection of the GTV boundaries in the EQD2 dose matrix. Since the GTV is different from the other structures in the conversion, a small jump in the EQD2 dose distribution should be detectable here. A jump is not visible in the profile curves shown at the GTV boundaries (*fig. 11*), since the dose is already approximately equal to the 2Gy prescription dose in the surrounding PTV fringe.

The most important test is the point-by-point recalculation of the biologically corrected EQD2 dose distribution. This test is also best performed in PlanEvaluation and showed good agreement at several test points. This can be easily understood from the graph provided (*fig. 12*).

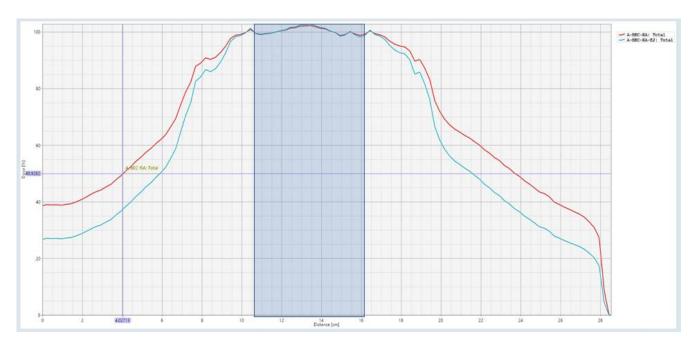


Fig. 12 Enlarged profile curve comparison between original dose (red) and EQD2 dose (blue) for recalculation of the biological dose correction. The shown point in the dose profile shows a dose value of 0.999Gy and lies in a range with $\alpha/\beta = 2$

At a prescribed fractional dose of 2Gy, the dose point in *fig. 12* shows a local nominal dose value of 0.999Gy (49.93%). Recalculated with the α/β -formula, α/β -value of 2 results in a local biological dose of 0.749Gy (37.45%) at this point, which corresponds to the value of the blue curve.

The EQD2 conversion was also tested for different fractionations, e.g. a 5 x 5Gy lumbal spine



Fig. 13 Comparison of original plan (left) and EQD2 converted evaluation plan (right) at 5 x 5Gy fractionation

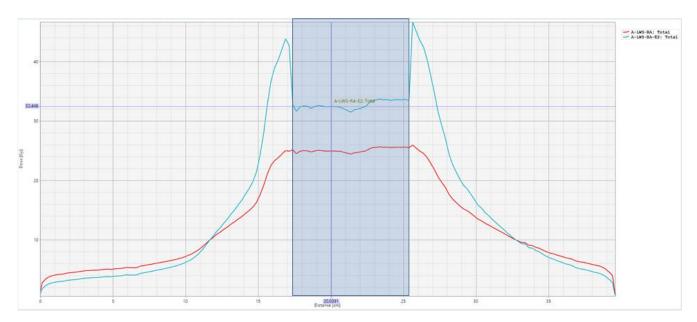


Fig. 14 Enlarged profile curve comparison between original dose (red) and EQD2 dose (blue) for recalculation of the biological dose correction of a 5 x 5Gy fractionation

When comparing the original and EQD2 dose for the 5 x 5Gy fractionation in *fig. 13*, a significantly larger EQD2 dose can be found in the volume surrounding the GTV.

Looking at the dose profiles of original plan and the EQD2 corrected dose (*fig. 14*), there is a steep increase seen for the blue EQD2 curve at the GTV edges due to the different α/β values of the tissues. Defining $\alpha/\beta = 8$ for the GTV (blue shaded region in *fig. 14*) in this case, the EQD2 calculation can be easily manually checked. For this example, the uncorrected dose inside the GTV (red curve) of 25Gy results in 32.5Gy EQD2 corrected dose.

The most frequent error in the prototype program was the failure to find different structures. This is due to the ID-specific structure assignment and will be corrected in the next program version by reading out and utilizing a structure list.

Conclusion and Outlook

These tests were performed on several patient plans and confirm the correct functioning of the ESAPI script EB_Bio3D . A clinical test run will be started. The published script is a prototype to demonstrate the procedure. In the next version, the previously defined α/β values in the code will be stored externally in an Excel file, which will serve as a config file. The current ID-specific structure assignment, also defined in the code, will be automated by a scanned structure list and subsequent substring evaluation.

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Availability and requirements

Project name: EB Bio3D

Project home page: https://github.com/EB-DOSIS/xxxx

Operating system(s): Windows10 Programming language: C#

Other requirements: Eclipse 15.6 incl. Eclipse Scripting API (VARIAN Medical

Systems), MS Excel 2017, MS Visual Studio Community 2019

License: free

Any restrictions to use by non-academics: At first only testing clinically in own

department (Radiotherapy of OGD Neuruppin)

List of abbreviations

DVH - Dose Volume Histogramm

DICOM - Digital Imaging and Communications in Medicine

ESAPI - Eclipse Scripting API

EQD2 - Equivalent dose in 2 Gy fractions

GTV - Gross Tumor Volume

IDE - Integrated Development Environment

PTV - Planning Target Volume

IDE - Integrated Development Environment

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and materials

See "Availability and requirements".

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

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