

# RegistrationShop: An Interactive 3D Medical Volume Registration System

Noeska N. Smit<sup>1</sup>, Berend Klein Haneveld<sup>1</sup>, Marius Staring<sup>2</sup>, Elmar Eisemann<sup>1</sup>, Charl P. Botha<sup>3</sup> and Anna Vilanova<sup>1</sup>

<sup>1</sup>Computer Graphics and Visualization group, Intelligent Systems, TU Delft, The Netherlands

<sup>2</sup>Division of Image Processing, Department of Radiology, LUMC, The Netherlands

<sup>3</sup>vxlabs, South Africa

---

## Abstract

*In medical imaging, registration is used to combine images containing information from different modalities or to track treatment effects over time in individual patients. Most registration software packages do not provide an easy-to-use interface that facilitates the use of registration. 2D visualization techniques are often used for visualizing 3D datasets.*

*RegistrationShop was developed to improve and ease the process of volume registration using 3D visualizations and intuitive interactive tools. It supports several basic visualizations of 3D volumetric data. Interactive rigid and non-rigid transformation tools can be used to manipulate the volumes and immediate visual feedback for all rigid transformation tools allows the user to examine the current result in real-time. In this context, we introduce 3D comparative visualization techniques, as well as a way of placing landmarks in 3D volumes. Finally, we evaluated our approach with domain experts, who underlined the potential and usefulness of RegistrationShop.*

Categories and Subject Descriptors (according to ACM CCS): I.3.8 [Computer Graphics]: Applications—

---

## 1. Introduction

3D medical imaging techniques like Magnetic Resonance Imaging (MRI) and X-ray Computed Tomography (CT) are increasingly used to study and diagnose diseases of patients [SBMJ\*12]. Often, follow-up scans are acquired to track the progression of a disease over time. However, comparing such datasets is difficult because the patient will never be in the exact same pose. In consequence, volumes are registered to establish image correspondences. Another application for registration is atlas-based segmentation [RBM\*05], in which a segmented dataset is registered to an unseen dataset, to transfer the segmentation. Registration is also useful for combining multi-modal images like Positron Emission Tomography (PET)/CT acquisitions with MRI scans. Each acquisition technique provides specific information that can aid diagnosis when properly combined. Additionally, even different scanners and acquisition techniques might lead to important variations.

Despite the broad spectrum of use cases for registration, there are currently not many free-to-use tools available that would be suitable for novice users, which contributes to the

fact that registration is not yet broadly used in a clinical setting. In particular, several available tools concentrate on the alignment of 2D slices, although registering volumes is a 3D operation. A transformation that appears perfectly aligned in 2D, might be misaligned in 3D. This restriction forces the user to construct and maintain a 3D mental model of the desired alignment transformations, which can be challenging.

Our goal is to provide a free and accessible 3D-3D registration solution. Our work, called *RegistrationShop*, facilitates the registration process by adding easy-to-use interaction techniques to existing state-of-the-art registration methods. Further, we provide interactive 3D visual feedback, which makes it easier for the user to recognize spatial relationships between datasets at a glance. Having a solution specifically designed for 3D-3D registration, leads to a less complicated interface compared to multipurpose tools and provides the user with a single solution to this tedious and difficult process. Our contributions are as follows:

- **The RegistrationShop system:** Our solution offers interactive transformation tools with instant visual feedback to iteratively improve the registration result. It introduces a

3D multi-volume rendering visualization to evaluate the registration in a single view as opposed to inspecting the result in linked individual views. RegistrationShop is distributed as open source under the MIT License and made available via GitHub.

- **The case-study-based evaluation:** We evaluated RegistrationShop via a user study with domain experts according to the guidelines for case study design by Yin [Yin94].

In the following, we will discuss related work and compare their features (Sec. 2) before describing RegistrationShop (Sec. 3) and its implementation (Sec. 4). A user study is presented (Sec. 5) before concluding (Sec. 6).

## 2. Related Work

Table 1 lists specific strengths and shortcomings of existing applications featuring registration functionality. The listed features are deemed requirements for a medical volume registration system. An ideal system would support multiple visualization options for individual datasets and the registration result (features 1 to 4). Furthermore, user-support for transformation definitions, such as landmark placement, and non-rigid registration should be available (features 5 to 7). A related visualization to inspect deformations after a non-rigid registration process should also exist (feature 8). GPU acceleration is a desirable feature to improve the speed of the registration process (feature 9) and the software should be free and multi-platform to allow for bigger uptake (feature 11 and 12).

There are three major commercial solutions. PMOD's Flexible Image Matching and Fusion Tool (PM) supports interactive rigid and non-rigid alignment of images. The user interface is complex and offers little explanation of functionality, but it can be upgraded to support a 3D external visualization [pmo96]. Mirada Medical (MR) uses fused 2D visualizations [Mir10]. It offers a manual interactive rigid registration and automatic rigid and non-rigid registration methods, including local partial registrations. FusionSync (FS) is a visualization and registration application by the Chimaera company [Chi13]. FusionSync lacks 3D visualization, but offers 2D investigation of multiple datasets and interactive rigid and non-rigid registration methods. It is only available for the aycan workstation OsiriX Pro.

Interestingly, free software solutions are usually multi-platform. AMIDE (AD), a Medical Image Data Examiner, uses fiducial markers (landmarks) and the maximization of mutual information for the registration process. Only rigid body transformation is supported. The software can also be used for viewing, and analyzing medical imaging datasets [LG\*03]. AMILab (AL) lacks landmark-based registration support and is an image processing application with visualization capabilities [KSSC\*12]. It is a multi-purpose and particularly supports multi-volume rendering. Slicer (SL) also allows to inspect, process and visualize 3D

image data [PHK04] and offers visualization (2D slices, 3D volume rendering) and registration (rigid and deformable) capabilities. It also supported multi-volume rendering in version 3.6, but this feature has been removed since version 4.0. Ezys (EZ) supports visualizations of multiple datasets and deformation fields. It is a non-linear 3D medical image registration program [GSA11], featuring 2D visualizations of multiple datasets and the deformation field. Non-rigid registrations in Ezys are GPU accelerated. The comparison step in VolView (VV) [Kit99], an open-source, advanced volume visualization tool, is a bit simpler; data sets are loaded next to each, but no multi-volume render possibilities exists. It also offers correlation based rigid registration and multi-modality registration methods.

General frameworks, such as Voreen (VR), facilitate open-source rapid application development for the interactive visualization and analysis of multi-modal volumetric datasets [MSRMH09]. Multi-volume rendering is possible through the inclusion of a template project, but the only way of interactively registering multiple volumes is by manually editing transformation matrices. MITK (MT) is used for building medical imaging applications [WVW\*04] and comes with the MITK workbench, which offers various functionalities in form of modules. Yet, the only available registration method is a non-rigid registration module — available only via custom builds.

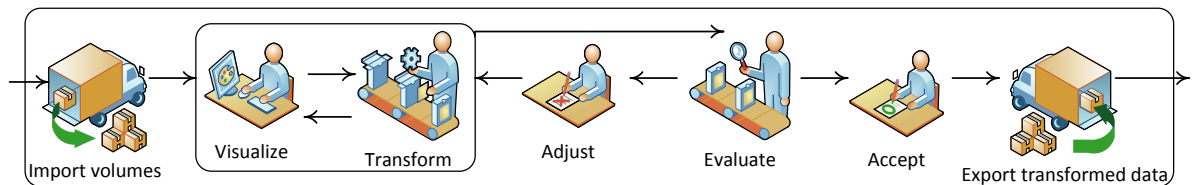
The commercial tools all are dedicated registration applications, whereas most non-commercial tools (except for Ezys) are volume visualization tools that are extended with registration functionality. Of these, Slicer and Ezys offer the most of the desired features. Unfortunately, Slicer is not specifically built for performing registrations and not easy to use for inexperienced users. Ezys lacks 3D visualization and rigid registration methods. It does feature GPU-accelerated non-rigid registration and is the only tool to feature visualizations of the deformation field. Table 1 shows that no solution currently combines all desired features.

## 3. RegistrationShop

This section describes the design of RegistrationShop by explaining the visualization capabilities and available interaction tools for manual landmark-based and automatic transformations. A high-level overview diagram of the registration process using RegistrationShop is given in Figure 1. First, the volumes to be registered are imported. Next, a 3D visualizations of the structures of interest provided and the user applies transformation tools to align the moving volume. Finally, the current registration results are evaluated and either accepted, leading to a transformed volume, or the transformations are adjusted again. The following subsections describe the most important stages in more detail.

	RS	AD	AL	FS	EZ	MT	MR	PM	SL	VV	VR
1. 3D volume visualization	✓	✓	✓	✗	✗	✓	✓ <sup>a</sup>	✗ <sup>b</sup>	✓	✓	✓
2. Multi-volume rendering	✓	✓	✓	✗	✗	✓	✗	✗ <sup>b</sup>	✗	✗	✓
3. Registration results inspection	2/3D	2/3D	3D	2D	2D	✗	2D	2/3D <sup>h</sup>	2D	✗	3D
4. 3D clipping of volumes	✓	✓	✓	✓	✗	✗	✓	✓	✓	✓	✗
5. Manual transformation	✓	✗	✓ <sup>c</sup>	✓	✗	✗	✓	✓	✓	✗	✓ <sup>d</sup>
6. Landmark transformation	✓	✓ <sup>e</sup>	✗	✗	✗	✗	✗	✓ <sup>f</sup>	✓	✗	✗
7. Non-rigid registration	✓	✓	✓	✓	✓	✓ <sup>g</sup>	✓	✓ <sup>h</sup>	✓	✓	✓
8. Deformation visualization	✗	✗	✗	✗	✓	✗	✗	✗	✗	✗	✗
9. GPU-accelerated registration	✓ <sup>i</sup>	✗	✗	✓	✓	✗	✗	✗	✗	✗	✗
10. Transformation history	✓	✗	✗	✗	✗	✗	✗	✗	✗	✗	✗
11. Free software	✓	✓	✓	✗	✓	✓	✗	✗	✓	✓	✓
12. Multiplatform	✓	✓	✓	✗	✓	✓	✗	✓	✓	✓	✓

**Table 1:** Features of RegistrationShop vs. related applications (alphabetical order): RS: RegistrationShop, AD: AMIDE, AL: AMILab, FS: FusionSync, EZ: Ezys, MT: MITK, MR: Mirada Medical, PM: PMOD, SL: Slicer, VV: VolView, VR: Voreen. <sup>a</sup>: MIP only. <sup>b</sup>: In external P3D tool. <sup>c</sup>: Functionality not working in current version 3.2.1. <sup>d</sup>: Interactive transformation matrix. <sup>e</sup>: Non-interactive landmark transformation wizard. <sup>f</sup>: Limited to only one set of landmarks. <sup>g</sup>: Not included by default in MITK workbench. <sup>h</sup>: Only available for brain normalization. <sup>i</sup>: Will become available with next Elastix release [SBL\*13].



**Figure 1:** A high-level overview diagram of performing a registration with RegistrationShop.

### 3.1. Visualizations

The visualization stage plays a central role, as the user sees in real-time how their transformations affect the registration results. Even small changes can be investigated and by responding to them, users converge, ultimately, to a solution.

#### 3.1.1. Color mapping

Throughout RegistrationShop the fixed volume is consistently shown as orange and the moving volume (to be registered) is shown in blue, as can be seen in Figure 2. This choice makes identifying the volumes easy in all stages. These specific colors were inspired by work on comparative 2D visualization [DBB\*13]. Being complementary colors, adding them results in a shade of gray whenever both are of the same intensity. If one intensity is higher, a shade of blue or orange will appear, making differences, as well as the identification of the volume causing the color, easy to spot. A second reason for this color scheme is that blue and orange can be distinguished by most colorblind people.

#### 3.1.2. Single volume visualizations

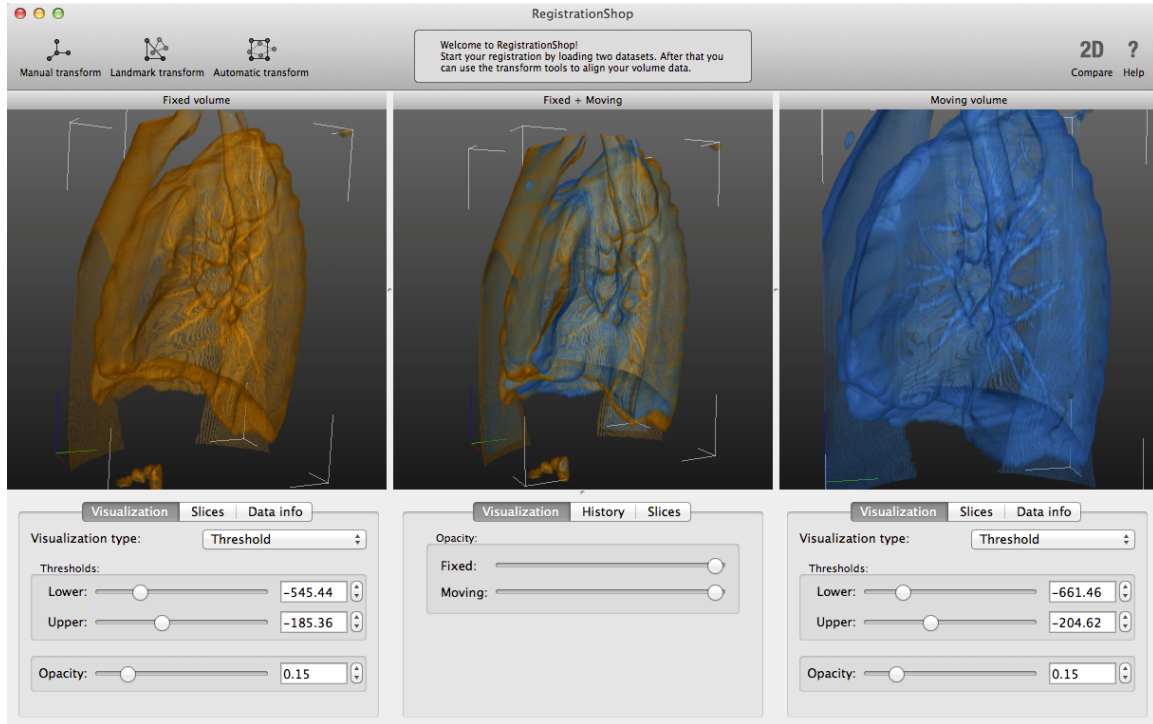
Two single-volume 3D-visualization options are available; the threshold visualization (THR) and Maximum Intensity Projection (MIP).

THR uses Direct Volume Rendering (DVR). To simplify controls for novice users, we offer only three sliders to define a transfer function. These modify a lower and upper threshold, as well as an opacity value. Figure 2 shows an example of a THR visualizations; orange, resp. blue, indicates the fixed, resp. moving, volume.

The second method, MIP, displays only the voxels with highest intensity along a ray from the camera. As for THR, data can be thresholded to exclude some voxels. This option makes MIP more flexible if high values in the data are not the values of interest.

#### 3.1.3. Multi-volume visualization

The view in the center of RegistrationShop fuses the adjacent fixed and moving view (left, right, respectively). One parameter, which can be adjusted for this view, is the opacity for each of the volumes to modify the blending process. This



**Figure 2:** Screenshot of the main interface of RegistrationShop displaying two CT lung datasets. Left: baseline data loaded as the fixed volume with the associated visualization parameters below. Right: follow-up data loaded as the moving volume. Center: multi-volume rendering the two volumes in a single visualization to reveal the current registration result with blending parameters below. The datasets are available from the Elastix test suite.

opacity parameter setting is then multiplied by the opacity based on the transfer function. Consequently, three visualization mixes are possible: THR-THR, THR-MIP, and MIP-MIP.

**THR-THR:** The transfer functions of the adjacent views are applied to the volumes and, during ray tracing, voxels from both volumes are sampled alternately, starting with the fixed volume. The technique for compositing the sampled values is the same as the technique used for standard ray tracing. An example is shown in Figure 2.

**MIP-THR:** When MIP and THR visualizations are combined, during ray tracing, intermediate values from the two volumes are maintained: the current maximum intensity for the MIP volume and the accumulated color and opacity value for the THR volume. These values are composited until the opacity value for the THR volume becomes saturated. An example is shown in Figure 3.

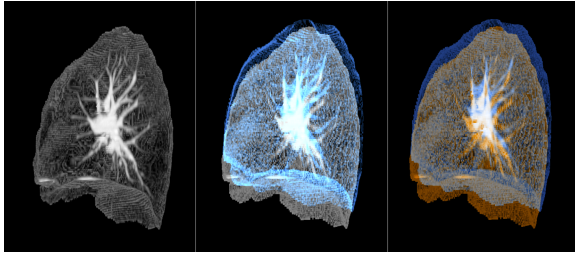
**MIP-MIP:** The combination of two MIP visualizations uses a technique that extends the 2D image blending method introduced by Dzyubackyk et al [DBB\*13]. Both of the volumes are separately traced with the MIP technique. The result of the fixed volume is transformed to orange while the

result of the moving volume is transformed to blue. These values are then added in RGB space. When the voxels of the volumes match well, the resulting image will exist of mainly gray values. In regions with differences, blue or orange will indicate mismatches, drawing the attention of the viewer to these locations (compare Figure 3).

A known disadvantage of the MIP technique is that it removes depth cues and volumes might seem to overlap perfectly from a certain angle, while, from a different viewpoint, it becomes apparent that the volumes do not match well. Interaction with the visualization is therefore needed to verify the result. In the future, it would be interesting to evaluate the use of MIDA instead of MIP in this comparison setting [BG09]. This fusion technique is mainly applicable to datasets of the same modality, as it relies on data similarity. Further, as maximum values along the ray are output, differences in lower value ranges are harder to spot.

### 3.1.4. 2D comparison tool

Domain experts working with image volumes are used to exploring volumetric data via 2D slices through the volume. Providing only a 3D visualization would ignore their previous experience and expertise. Hence, we also include a 2D



**Figure 3:** Examples of visualizations in RegistrationShop. Left: a single volume rendered with MIP. Center: two volumes rendered combining MIP with THR. Right: two volumes rendered combining MIP with MIP. The two rightmost figures reveal that the two volumes are currently not aligned.

comparison tool to verify results acquired with the 3D registration.

A secondary reason for 2D visualization is to provide means for a detailed inspection, as it provides a direct view of the data. In a 3D visualization, the data is filtered through color and opacity assignment and details of the original datasets might no longer be visible in 3D. The layout of the views is the same as in the 3D viewer (Figure 4).

### 3.2. Transformation tools

To transform the moving volume, we included a manual, a landmark-based, and an automatic transformation tool. Whenever a tool is applied, the modification is kept in a history tab to allow the user to compare, or undo previous operations. This history tab stores all steps performed in the registration pipeline for the current project and can be used to visually inspect the results of previous steps.

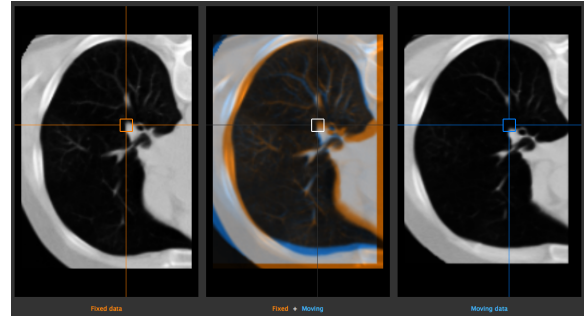
#### 3.2.1. Manual transformation tool

The manual transformation is used to coarsely align data sets and can serve as an initialization for subsequent registration steps. Here, the user interacts with a box widget, making interactive rigid transformations, rotations, and scaling of the moving volume possible.

#### 3.2.2. Landmark-based transformations

Landmarks can be used to register mutual correspondence points in both volumes. A least-squares fit is then used to find a best match between corresponding landmark positions. The computation is interactive and builds upon the unit-quaternion algorithm by Horn [Hor87], which offers the choice between rigid, similarity-based, or affine transformations.

When specifying a landmark, the location is marked with a sphere and an additional circle around it. The sphere is drawn in the context of the volume, while the circle is drawn



**Figure 4:** 2D comparison tool with the lung datasets. Left: the fixed volume. Center: the current registration result. Right: the moving volume.

as an overlay, hence, keeping it always visible. Landmarks are specified in pairs and whenever a new landmark pair is indicated, the transformation is updated and its effect instantly shown in the multi-volume view.

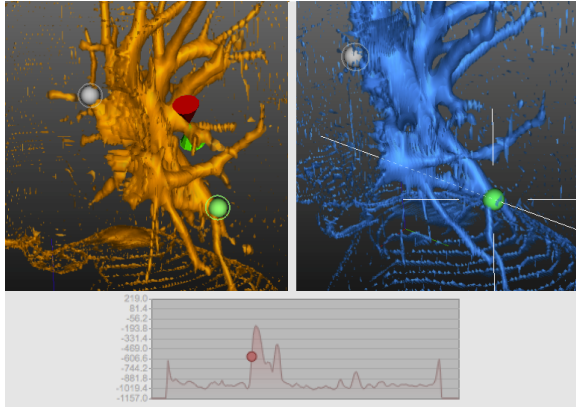
Placing landmarks in a volume is not a trivial procedure: there are three dimensions in a volume, which are displayed on a two dimensional screen. Further, to ensure a wide use of our software, we restricted ourselves to mouse interaction, but, this choice, leads to 2D coordinates in screen space. Due to possible voxel transparency, it is impossible to know exactly, which voxel a user chooses based on a 2D DVR image. To remedy this problem, we offer two solutions: the surface picker and the two-step picker.

The **surface picker** traces a ray through the volume, originating from the mouse position, to determine the first voxel with an opacity value that exceeds a pre-defined threshold value. At this location, two cones, aligned with the normal (gradient) of this location, giving the impression that one cone appears to stick out of the surface, while the other seems to disappear behind it. The cones are rendered in the same context as the volume, giving the user a sense of the chosen voxel's depth (Figure 5).

The **two-step picker** addresses cases in which the surface picker potentially fails; e.g., if the opacity of the intended location is below the threshold, or a higher opacity region occludes it. The principle of the two-step picker relates to stereo reconstruction. In the first step, the user selects a location on screen to which the intended voxel projects, hereby, effectively restricting its location to the corresponding ray through the volume. In the second step, a different view is chosen and, again, the projected location of the intended voxel is clicked. The algorithm will then choose the point on the first line, closest to the second.

A sphere is used to indicate the selected location along the first line. Additionally, to support the user in the selection process, the depth profile along the first ray and the current selection is shown in the volume view (Figure 5). The inten-





**Figure 5:** Landmark transformation tools. Left: surface picker (red and green cone) with an active (green) landmark and an inactive (gray) landmark. Right: two-step picker after shooting the picking ray. Bottom: associated value-profile along the ray for the two-step picker.

sity profile embeds the location in a context and can also be used directly to drive the selection.

### 3.2.3. Automatic transformation tool

The automatic transformation tool in RegistrationShop is a wrapper around the command-line version of Elastix, an open-source library with which rigid and non-rigid registration algorithms can be executed [KSM\*10]. Elastix, while powerful, can be difficult to use for non-technical users due to the command-line interface and complexity of the parameter file choices. RegistrationShop provides default parameter files to start the registration process, which hides the technicalities from the user. Nonetheless, additional custom parameter files can be loaded or created. If an initial rigid transformation has been produced in RegistrationShop, it will be passed to Elastix to initiate the optimization. When Elastix finishes the registration, the created dataset is displayed automatically in RegistrationShop. The registration result can then be evaluated and corrected if needed.

## 4. Implementation

RegistrationShop uses several languages and frameworks. It is written in Python using the Visualization Toolkit (VTK) and PySide. VTK was chosen because of its volume-rendering and loading capabilities. PySide was used for building the user interface because it allows cross-platform development targeting all major platforms.

VTK does not support rendering of multiple volumes by default and we used a custom extension created by K. Krisian and C. Falcón-Torres [KFT]. The code has been adjusted and extended for all the possible combinations of DVR and MIP visualizations.

	MR	RA	I1	I2
Registration frequency	low	avg.	avg.	high
3D experience	low	avg.	high	high
Elastix experience	low	low	high	high
Technical knowledge	avg.	low	high	high

**Table 2:** Domain experts’ prior experience (avg.: average).

As indicated, Elastix is used for the non-rigid registration. It is based on The Insight Segmentation and Registration Toolkit (ITK), so it shares most of its functionality. Elastix is distributed under the simplified BSD-license. Elastix was the framework of choice as it has a permissive license.

Alternatively, we could have used ITK, which is an open-source, cross-platform segmentation solution [YAL\*02], or DROP, which uses Markov Random Fields (MRF) to optimize for cost functions [GKT\*08]. Compared to the gradient-descent method in Elastix, it performs well and is a promising alternative, but licensing allows only for research and non-commercial purposes.

## 5. Evaluation

We relied on an evaluation by experts to evaluate if RegistrationShop reaches its goals of making the registration process easier and is able to produce the desired/intended result. We rely on two case studies with medical domain experts, who compared RegistrationShop to their current registration workflow.

### 5.1. Case study design

Our case-study design follows the guidelines in [Yin94]. The main evaluation question has been formulated as follows: “Does RegistrationShop make performing registrations easier and help in producing the desired/intended result by providing 3D visualizations of the datasets in combination with simple interactive tools with instant user feedback?”.

Participants were a medical radiation therapist (MR), a radiologist (RA) and two image-processing experts (I1, I2), who are all familiar with medical image registration. The first two experts are more familiar with the medical applications of registration, while the latter two are experts in registration itself. These experts were chosen to have a reasonable coverage of users who might be interested in using RegistrationShop. Before starting, the domain experts were asked to answer several questions about their prior knowledge and experiences with registration, which allowed us to investigate the level of technical expertise in dealing with 3D visualization and interaction. Based on these questions, levels of prior experience were defined for all four domain experts (Table 2). MR does not perform registration in his current work or possess any prior knowledge on 3D visualization and interaction. While having some technical knowl-

edge, MR is not familiar with Elastix. RA performs registrations automatically, using a radiologist workstation, and was also not familiar with Elastix. RA does use 3D visualization techniques occasionally, but is not familiar with technical terms. The two image processing experts I1 and I2 both are familiar with 3D visualizations, Elastix and technical terms. The only difference in prior experience between them is that I2 performs registrations more frequently.

Each evaluation session took 40 minutes and consisted of three phases. In the first phase, we showed the expert a live demonstration of the RegistrationShop system by registering test volumes containing misaligned 3D cubes. In the second phase, the expert was asked to perform a registration on a dataset from clinical practice. Two of the experts were asked to register full-body MRI scans of the same patient at different time-points, while the last two experts were asked to align baseline and follow-up CT-scans of a lung. These datasets were chosen, because they were closest to the type of studies currently performed by the users. We encouraged the experts to think out loud during this process and recorded the audio and screen. During the third phase, we asked the expert to express their level of agreement to the statements on a five-point Likert scale and to provide vocal commentary to clarify their responses.

## 5.2. Case study results

To examine our hypothesis, we decomposed the main evaluation question into several related propositions that the domain experts were asked to respond to after using RegistrationShop (Table 3).

### 5.2.1. 3D visualizations

The 3D visualizations of the datasets were regarded as interesting and succeeded in providing a sense of the overall anatomical structure of the data and the spatial relations between the two volumes (question 17). Three users indicated that the inspection of the data is simplified by the visualization capabilities of RegistrationShop, although one image processing expert found 2D inspection easier (question 3) and also prefers to evaluate registration results in 2D (question 17). The combined viewer was successful in showing the spatial relation between the datasets, especially, because of the instant user feedback when working with the transformation tools. Because some domain experts were not familiar with interaction in 3D, they indicated that they would not consider navigation easy and expect a learning curve (questions 1, 2). Making a meaningful 3D visualization was also not considered easy by two experts due to a learning curve, but also lacking features, such as a reset functionality or optional parameter and camera linking (question 5). Two experts strongly agree that the single-volume 3D visualizations help to display internal structures of the data, but one expert pointed out that for the full-body MRI volumes,

internal structures cannot be shown easily using volume rendering techniques. One expert indicated he could not visualize internal details of the lung dataset easily (question 4). While the 3D visualization is suitable for displaying anatomical structures, it is less suitable for detailed voxel-by-voxel inspection and comparison of the datasets. All experts agree that a 2D visualization is required for detailed inspection; consequently, the inclusion of the 2D comparison tool was deemed necessary (questions 18, 19). Incorporation of the 2D comparison tool in the 3D views was suggested as a potential improvement. Three experts suggested other improvements when asked if RegistrationShop provides them with all the tools they need for registration (question 21). Additional features included deformation-field visualization for non-rigid registrations, measurements and statistical reports of the datasets, and interactive segmentation.

### 5.2.2. Transformation tools

The transformation tools were mostly successful in helping the experts to create registrations, though one expert experienced problems when using the manual box widget for rotations (question 6). All experts agreed or strongly agreed that the manual transform tool is able to create a good initialization for subsequent registration steps (question 8). Landmark placement allowed the users to indicate the intended locations, though one expert would have liked to place landmarks in the 2D view as well (question 10). Especially landmark placement using the two-step picker was deemed useful; its value-profile visualization was considered helpful to determine the correct placement in 3D (question 12). However, the visualization of the surface picker and the landmarks should not obstruct the indicated location (question 9). The real-time transformation updates were appreciated by all and allowed the experts to understand landmark placement effects (question 11). The history tab allowed the experts to assess if a registration step had improved the registration result, and the combination with the real-time interaction updates was considered helpful by the experts (question 20).

### 5.2.3. Elastix

The image processing experts familiar with Elastix (I1 and I2) appreciated the interaction between RegistrationShop and Elastix and the choice of default and custom parameter files (questions 14, 15). The parameter editing was considered easier in RegistrationShop by one expert (question 16). The other expert has such extensive experience with Elastix, he found that it did not make working with Elastix easier for him personally. He did comment that RegistrationShop would be valuable to inexperienced users or users that infrequently do registrations. The benefit of using RegistrationShop over Elastix is that the results of an Elastix run can be visually inspected immediately after completion.

Statement	MR	RA	I1	I2
1. Navigation is quick and easy.	4	2	2	3
2. Navigation controls are clear and easy to get used to.	4	4	2	3
3. Inspection of the data is simplified by the visualization capabilities.	4	4	2	4
4. The single-volume 3D visualizations help display internal structures of the datasets.	5	1	2	5
5. It is easy to make a meaningful 3D visualization with the available visualization options.	5	1	3	2
6. The interactive box allows for quick and easy dataset alignment.	4	1	4	4
7. The interactive transformation matrix is a useful optional tool.	N/A	N/A	2	1
8. A manual transform made with RegistrationShop is a good initialization.	5	4	4	5
9. The surface picker allows for quick landmark placement in the intended locations.	3	3	2	3.5
10. The 3D visualizations enable placement of the landmarks in the intended locations.	4	4	4	3
11. Real-time updates in the combined view demonstrate landmark placement effects.	4	4	5	5
12. The two-step picker works where the surface picker would fail.	4	N/A	5	5
13. Making an initial transform for Elastix is easy with RegistrationShop.	N/A	N/A	N/A	2.5
14. Loading Elastix parameter files enables re-use of existing work.	N/A	N/A	N/A	5
15. The standard Elastix parameters are a good starting point for deformable registration.	N/A	N/A	4	5
16. Adjusting parameter values for Elastix is easier in RegistrationShop.	N/A	N/A	4	1
17. The 3D multi-volume visualization allows me to evaluate registration results.	5	4	2	5
18. The 2D comparison tool is indispensable to evaluate registration results.	5	4	4	5
19. The need for 2D visualizations is reduced by the 3D visualizations.	2	1	1	1
20. The history tab allows me to see if the registration improved with a registration step.	3	4	4	5
21. RegistrationShop provides me with all the tools I need to perform a registration.	2	2	2	5
22. I do not need additional technical knowledge to operate RegistrationShop	4	4	N/A	N/A
23. I see myself using RegistrationShop in the future.	3	3	4	5

**Table 3:** Domain expert level of agreement with statements based on a Likert scale. 1: Strongly disagree, 2: Disagree, 3: Neither agree nor disagree, 4: Agree, 5: Strongly agree, N/A: Not available. The x.5 values were given where the user did not feel the five-point Likert scale could reflect his opinion accurately.

### 5.2.4. Conclusion

Overall, RegistrationShop was well received by the users. The interface was praised by one of the non-technical experts for its simplicity and clear layout. The domain experts with limited technical experience experts felt that using RegistrationShop does not require additional technical knowledge, while the image processing experts could not answer as they already possess the corresponding technical knowledge (question 22). MR remarked that when previously using other registration software, it took four days to get acquainted with the tool, while RegistrationShop allows a user to get results quickly and intuitively. The image processing experts both could see themselves using RegistrationShop in the future, while the clinicians neither agreed nor disagreed with this statement, because their current work does not require them to manually register datasets (question 23).

The user study indicates that in regard to our main evaluation question, several preliminary results can be reported. The 3D visualization is appreciated, but requires integration with a detailed 2D inspection of the volumes and registration result. Furthermore, the simple interactive transformation tools got positive feedback from all four users. Finally, the instant visual user feedback was found helpful to evaluate the result of transformation interactions on the registration outcome. The non-technical experts found that they

do not need additional technical knowledge to operate RegistrationShop. The image processing experts consider our work a promising volume registration tool with the potential to make registration more accessible to clinicians and researchers in the future.

### 6. Conclusion and Future Work

We presented RegistrationShop, a 3D-3D volume registration system making use of 3D visualizations for the moving and fixed volumes alongside the current registration result. It provides a set of interactive tools coupled with instant visual feedback, which helps the user to iteratively register the datasets, as underlined by the appreciation of experts that evaluated our system.

Despite the overall positive outcome of our study, there is still room for future work, such as the integration of 2D views in the 3D volume, region-of-interest tools, such as special lenses or segmentation tools to visualize mutual information about the registration quality in certain regions. Similarly, other compositing operations [SS11] or transfer function definition could be used [HBKG08, BBB\*12]. We also envision using new saliency and similarity measures to further improve the landmark placing process [AXPA06]. Furthermore, a larger follow-up user study is needed to further examine the clinical potential of RegistrationShop.



Visualizing the non-rigid deformation field might be helpful and lead to a more-likely acceptance in a clinical setting. Several users indicated this potential of our work, especially, as it makes the complicated task of registration less complex and accessible to inexperienced users.

RegistrationShop is freely available as an open source prototype and the source code of RegistrationShop can be viewed and downloaded on GitHub.

## Acknowledgements

The full body MRI data used in the evaluation sessions was provided courtesy of the division of Image Processing, Department of Radiology of the Leiden University Medical Center. The CT lung data presented in this article was provided courtesy of the Elastix test suite. This work is supported by the Technology Foundation STW.

## References

- [AXPA06] AZAR A., XU C., PENNEC X., AYACHE N.: An interactive hybrid non-rigid registration framework for 3d medical images. In *Biomedical Imaging: Nano to Macro, 2006. 3rd IEEE International Symposium on* (2006), IEEE, pp. 824–827. 8
- [BBB\*12] BRAMON R., BOADA I., BARDERA A., RODRIGUEZ J., FEIXAS M., PUIG J., SBERT M.: Multimodal data fusion based on mutual information. *IEEE Transactions on Visualization and Computer Graphics* 18, 9 (Sept. 2012), 1574–1587. 8
- [BG09] BRUCKNER S., GRÖLLER M. E.: Instant volume visualization using maximum intensity difference accumulation. *Computer Graphics Forum* 28, 3 (2009), 775–782. 4
- [Chi13] Chimaera - fusionsync. URL: <http://www.chimaera.de/chimaera/applications/fusionsync.html>, 2013. Accessed: 2014-05-25. 2
- [DBB\*13] DZYUBACHYK O., BLAAS J., BOTHA C. P., STARING M., REIJNIERSE M., BLOEM J. L., VAN DER GEEST R. J., LELIEVELDT B. P.: Comparative exploration of whole-body mr through locally rigid transforms. *International journal of computer assisted radiology and surgery* 8, 4 (2013), 635–647. 3, 4
- [GKT\*08] GLOCKER B., KOMODAKIS N., TZIRITAS G., NAVAB N., PARAGIOS N.: Dense image registration through mrfs and efficient linear programming. *Medical Image Analysis* 12, 6 (2008), 731–741. 6
- [GSA11] GRUSLYS A., SAWIAK S., ANSORGE R.: 3000 non-rigid medical image registrations overnight on a single pc. In *Nuclear Science Symposium and Medical Imaging Conference (NSS/MIC), 2011 IEEE* (2011), IEEE, pp. 3073–3080. 2
- [HBKG08] HAIDACHER M., BRUCKNER S., KANITSAR A., GRÄÜLLER M. E.: Information-based transfer functions for multimodal visualization. In *Proceedings of the First Eurographics Conference on Visual Computing for Biomedicine* (2008), EG VCBM'08, Eurographics Association, pp. 101–108. 8
- [Hor87] HORN B. K.: Closed-form solution of absolute orientation using unit quaternions. *JOSA A* 4, 4 (1987), 629–642. 5
- [KFT] KRISSIAN K., FALCÓN-TORRES C.: GPU volume ray casting of two volumes within VTK. URL: <http://hdl.handle.net/10380/3350>. Accessed: 2014-05-25. 6
- [Kit99] Kitware, inc. - volview. URL: <http://www.kitware.com/opensource/volview.html>, 1999. Accessed: 2014-05-25. 2
- [KSM\*10] KLEIN S., STARING M., MURPHY K., VIERGEVER M. A., PLUIM J. P.: Elastix: a toolbox for intensity-based medical image registration. *Medical Imaging, IEEE Transactions on* 29, 1 (2010), 196–205. 6
- [KSSC\*12] KRISSIAN K., SANTANA F., SANTANA-CEDRÉS D., ET AL.: Amilab software: medical image analysis, processing and visualization. *Medicine Meets Virtual Reality-NextMed (MMVR). CA, USA: IOS Press* 173 (2012), 233–237. 2
- [LG\*03] LOENING A. M., GAMBHIR S. S., ET AL.: Amide: a free software tool for multimodality medical image analysis. *Molecular imaging* 2, 3 (2003), 131–137. 2
- [Mir10] Mirada medical ltd. medical imaging software for radiation oncology and diagnostic radiology. URL: <http://www.mirada-medical.com/>, 2010. Accessed: 2014-05-25. 2
- [MSRMH09] MEYER-SPRADOW J., ROPINSKI T., MENSCHMANN J., HINRICHS K.: Voreen: A rapid-prototyping environment for ray-casting-based volume visualizations. *Computer Graphics and Applications, IEEE* 29, 6 (2009), 6–13. 2
- [PHK04] PIEPER S., HALLE M., KIKINIS R.: 3d slicer. In *Biomedical Imaging: Nano to Macro, 2004. IEEE International Symposium on* (2004), IEEE, pp. 632–635. 2
- [pmo96] Pmod technologies ltd. - pmod image fusion. URL: [http://www.pmod.com/technologies/products/image\\_fusion/image\\_fusion.php](http://www.pmod.com/technologies/products/image_fusion/image_fusion.php), 1996. Accessed: 2014-05-25. 2
- [RBM\*05] ROHLFING T., BRANDT R., MENZEL R., RUSAKOFF D. B., MAURER JR C. R.: Quo vadis, atlas-based segmentation? In *Handbook of Biomedical Image Analysis*. Springer, 2005, pp. 435–486. 1
- [SBL\*13] SHAMONIN D. P., BRON E. E., LELIEVELDT B. P., SMITS M., KLEIN S., STARING M., INITIATIVE A. D. N., ET AL.: Fast parallel image registration on cpu and gpu for diagnostic classification of alzheimer's disease. *Frontiers in neuroinformatics* 7 (2013). 3
- [SBMJ\*12] SMITH-BINDMAN R., MIGLIORETTI D. L., JOHNSON E., LEE C., FEIGELSON H. S., FLYNN M., GREENLEE R. T., KRUGER R. L., HORN BROOK M. C., ROBLIN D., ET AL.: Use of diagnostic imaging studies and associated radiation exposure for patients enrolled in large integrated health care systems, 1996-2010. *Jama* 307, 22 (2012), 2400–2409. 1
- [SS11] SCHUBERT N., SCHOLL I.: Comparing gpu-based multi-volume ray casting techniques. *Computer Science-Research and Development* 26, 1-2 (2011), 39–50. 8
- [VWV\*04] WOLF I., VETTER M., WEGNER I., NOLDEN M., BOTTGER T., HASTENTEUFEL M., SCHOBINGER M., KUNERT T., MEINZER H.-P.: The medical imaging interaction toolkit (mitk): a toolkit facilitating the creation of interactive software by extending vtk and itk. In *Medical Imaging 2004* (2004), International Society for Optics and Photonics, pp. 16–27. 2
- [YAL\*02] YOO T. S., ACKERMAN M. J., LORENSEN W. E., SCHROEDER W., CHALANA V., AYLWARD S., METAXAS D., WHITAKER R.: Engineering and algorithm design for an image processing api: a technical report on itk-the insight toolkit. *Studies in health technology and informatics* (2002), 586–592. 6
- [Yin94] YIN R. K.: *Case Study Research: Design and Methods*. Thousand Oaks, CA: Sage, 1994. 2, 6