# Package 'neuroSCC'

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Title Estimation of SCC's for PET Neuroimaging Data
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<b>Description</b> This package provides functions for the estimation of Simultaneous Confidence Corridors (SCCs) on PET neuroimaging data. It is designed to help with the replication of methods implemented in the Ph.D. Thesis `Development of statistical methods for neuroimage data analysis towards early diagnostic of neurodegenerative diseases" and it is best applied using the scripts available in the link below. Further information on the methodology for SCCs estimation can be found in: ``Wang Y, Wang G, Wang L, Ogden RT. Simultaneous confidence corridors for mean functions in functional data analysis of imaging data. Biometrics. 2020 Jun;76(2):427-437".
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databaseCreator

Create a database of processed PET image data

#### **Description**

This function automates the processing of PET images based on a specified file name pattern within a working directory. It reads each file matching the pattern, processes it using neuroCleaner, and compiles the results into a comprehensive data frame. The function serves as a key step in the neuroSCC workflow, bridging between individual image processing and preparation for functional data analysis with Simultaneous Confidence Corridors.

## Usage

```
databaseCreator(
  pattern,
  control = TRUE,
  extractPattern = NULL,
  useSequentialNumbering = FALSE,
  demo = NULL,
  quiet = FALSE
)
```

#### **Arguments**

pattern character, a regular expression pattern that specifies which files to process.

By default, the function is designed to work with filenames structured like: "masked\_swwwC1\_tripleNormEsp\_roiAD\_0\_1\_rrec\_OSEM3D\_32\_it1.nii", where

"C1" indicates the subject identifier.

control logical, if TRUE, the function processes control group images and if FALSE, it

processes pathological group images. Default is TRUE.

extractPattern character, optional custom regular expression to extract the subject number

from filenames. Should contain a capture group (\d+) to extract the numerical

ID. Default is NULL, which uses the built-in pattern "masked\_swwwC(\d+)\_.\*".

use Sequential Numbering

logical, if TRUE, assigns sequential numbers (1,2,3,...) to files instead of at-

tempting to extract numbers from filenames. Default is FALSE.

demo data.frame, optional demographic data formatted according to the demoCleaner

function. If provided, this demographic information will be included in the out-

put database for each file. Default is NULL.

quiet logical, if TRUE, suppresses progress messages. Default is FALSE.

#### **Details**

The function performs several key operations:

- 1. Identifies files in the working directory that match the specified pattern
- 2. For each matching file: a. Extracts the subject number from the filename or assigns a sequential number b. Processes the file using neuroCleaner, including demographic data if provided c. Adds subject identifier information to each row d. Appends the data to a growing database

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The subject number extraction uses either:

- The custom pattern provided in extractPattern
- Sequential numbering (1,2,3,...) if useSequentialNumbering=TRUE
- The default pattern "masked\_swwwC(\d+)\_.\*" which extracts numbers after "C" in filenames

This function is typically followed by matrixCreator in the analysis pipeline, which transforms the database into a format suitable for SCC computation.

#### Value

A data. frame that aggregates processed data from each image. Each row represents data from one voxel (3D pixel), including:

- For control group (control=TRUE): CN\_number, z, x, y, pet
- For pathological group (control=FALSE): AD\_number, z, x, y, pet
- If demographic data is provided: Additional columns like PPT, Group, Sex, Age will be included

The CN\_number or AD\_number column contains the subject identifier extracted from the filename or assigned sequentially. The pet column contains the intensity values.

#### See Also

neuroCleaner for the underlying image processing function.

matrixCreator for the next step in the workflow that converts the database to a matrix format for SCC analysis.

#### **Examples**

```
# Example 1: Basic usage with default settings for control group
## Not run:
# Set the working directory where your PET images are stored
setwd("~/PET_Images")
# Define the pattern for file names to process
pattern <- "^masked_swwwC\\d+_tripleNormEsp_w00_rrec_OSEM3D_32_it1.nii"</pre>
# Create the database for control group images
database_CN <- databaseCreator(pattern, control = TRUE)</pre>
# Example output (first few rows):
\# CN_number z x y
     35 1
35 1
# 1
                        1
                              0.0
                      1
2
# 1
                              0.0
            35 1 3
                              2.3
# 1
# ...
## End(Not run)
# Example 2: Using demographic data
## Not run:
# Load demographic data
demo_data <- read.csv("demographics.csv")</pre>
```

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```
# Create database with demographic information
database_CN <- databaseCreator(pattern, control = TRUE, demo = demo_data)</pre>
# Example output with demographic data:
# PPT
         Group Sex Age CN_number z
                                                      pet
        Control M 65 1
# P001
                                          1
                                      35
                                                 1
                                                       0.0
                                               2
# P001
        Control M 65 1
                                     35 1
                                                       0.0
# P001 Control M 65 1
                                    35
                                          1
                                               3
                                                       2.3
# . . . .
## End(Not run)
# Example 3: Processing pathological group images
## Not run:
# Define the pattern for pathological images
pattern <- "^masked_swwwC\\d+_tripleNormEsp_roiAD_0_8_rrec_OSEM3D_32_it1.nii"</pre>
# Create the database for pathological group images
database_AD <- databaseCreator(pattern, control = FALSE)</pre>
# Example output (first few rows):
# AD_number z x
                              pet
                       У
# 1
             35
                   1
                        1
                              0.0
                      2
            35
# 1
                   1
                              0.0
                      3
             35 1
# 1
                              1.8
# ...
## End(Not run)
# Example 4: Using a custom extraction pattern
## Not run:
# For files named like "subject_023_scan.nii"
pattern <- "^subject_\\d+_scan.nii"</pre>
extractPattern <- "subject_(\\d+)_scan"</pre>
database <- databaseCreator(pattern, extractPattern = extractPattern)</pre>
## End(Not run)
# Example 5: Using sequential numbering instead of extracting from filenames
## Not run:
# For files that don't contain subject numbers in their names
pattern <- "^pet_scan_.*\\.nii"</pre>
database <- databaseCreator(pattern, useSequentialNumbering = TRUE)</pre>
## End(Not run)
# Example 6: Reproducible example with synthetic data
if (requireNamespace("oro.nifti", quietly = TRUE)) {
  # Create temporary directory and files for demonstration
  temp_dir <- tempdir()</pre>
  old_dir <- getwd()</pre>
  setwd(temp_dir)
  # Create two simple synthetic NIFTI files
  for (i in 1:2) {
```

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```
# Create a small synthetic array (3x3x3)
img_data <- array(1:27, dim = c(3, 3, 3))
nii_obj <- oro.nifti::nifti(img_data)

# Save with names that match our expected pattern
filename <- paste0("masked_swwwC", i, "_tripleNormEsp_w00_rrec_OSEM3D_32_it1.nii")
oro.nifti::writeNIfTI(nii_obj, filename = file.path(temp_dir, filename), verbose = FALSE)
}

# Process these files
pattern <- "^masked_swwwC\\d+_tripleNormEsp_w00_rrec_OSEM3D_32_it1.nii"
# This will not run if oro.nifti is not installed
# database <- databaseCreator(pattern)

# Clean up and restore working directory
setwd(old_dir)
}</pre>
```

getDimensions

Get Dimensions from a Neuroimaging File

#### **Description**

Extracts dimensional information from NIFTI or similar neuroimaging files. This function is designed to work together with neuroCleaner() but can also be used independently for informative purposes.

#### Usage

```
getDimensions(file)
```

#### **Arguments**

file

A NIFTI file object or filename to extract dimensions from.

#### **Details**

The function can handle both NIFTI file paths and pre-loaded oro.nifti file objects. It provides a consistent way to extract dimensional information across the package.

#### Value

A list containing:

- xDim: Number of voxels in the X dimension
- yDim: Number of voxels in the Y dimension
- zDim: Number of slices in the Z dimension
- dim: Total number of voxels (xDim \* yDim)

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#### **Examples**

```
## Not run:
# Using a file path
dims <- neuroSCC::getDimensions("path/to/your/image.nii")
# If used within neuroCleaner
file <- oro.nifti::readNIfTI("path/to/your/image.nii")
dims <- neuroSCC::getDimensions(file)
## End(Not run)</pre>
```

getPoints

Extract significant SCC points from an SCC comparison object

#### **Description**

This function identifies and extracts coordinates where significant differences fall outside the simultaneous confidence corridors (SCCs). It processes the results from ImageSCC::scc.image, returning the extracted coordinates where the differences are statistically significant.

#### Usage

```
getPoints(sccResult)
```

#### **Arguments**

sccResult

A list containing SCC computation results from ImageSCC::scc.image. The list should include at least:

- Z.band: Matrix specifying grid positions.
- ind.inside.cover: Indices of grid points inside the confidence band.
- scc: 3D array containing computed SCC values.

## **Details**

- Positive points indicate where the first group (e.g., Control) is significantly stronger.
- Negative points indicate where the second group (e.g., Pathological) is significantly stronger.
- This function must be used **after** running ImageSCC::scc.image.

#### Value

A named list:

- positivePoints: Data frame with coordinates where the first group shows significantly higher values than the second.
- negativePoints: Data frame with coordinates where the second group shows significantly higher values than the first.

## See Also

ImageSCC::scc.image for SCC computation.

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#### **Examples**

```
## Not run:
# Load SCC results (previously computed)
load("SCC_COMP.RData")

# Extract significant SCC points
significantPoints <- getPoints(SCC_COMP)

# Display extracted coordinates
head(significantPoints$positivePoints) # External significant points
head(significantPoints$negativePoints) # Internal significant points (if any)
## End(Not run)</pre>
```

matrixCreator

Convert database from PET image data to a functional data matrix format

#### Description

This function transforms a database created by databaseCreator into a matrix format suitable for functional data analysis. Each row of the matrix represents a subject's (patient or control) PET data, formatted as a continuous line of data points to simulate a functional representation.

#### Usage

```
matrixCreator(
  database,
  pattern = NULL,
  paramZ = 35,
  extractPattern = NULL,
  useSequentialNumbering = FALSE,
  quiet = FALSE
)
```

#### **Arguments**

database A data frame created by databaseCreator containing PET image data with

columns for group number, z, x, y, and pet values.

pattern The regular expression pattern used to match filenames in the database. This

should correspond to the naming conventions of the PET image files processed

by databaseCreator.

paramZ The specific z-coordinate slice to analyze. Default is 35.

extractPattern Optional custom regular expression to extract subject numbers from filenames.

Should contain a capture group for numerical ID.

useSequentialNumbering

If TRUE, assigns sequential numbers instead of extracting from filenames.

quiet If TRUE, suppresses progress messages.

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#### **Details**

This function is a critical step in the neuroSCC workflow for preparing data for Simultaneous Confidence Corridors (SCC) analysis. It performs several key operations:

- 1. Verifies the existence of the specified z-slice in the input database
- 2. Automatically calculates matrix dimensions based on the x and y coordinates of the specified z-slice
- 3. Extracts PET intensity values for each subject at the specified z-slice
- 4. Handles different group types (control or pathological) by recognizing appropriate identification columns
- 5. Provides flexible subject number extraction:
  - Uses a provided custom pattern
  - · Falls back to sequential numbering
  - Supports default filename-based number extraction
- 6. Replaces any NaN values with zero to ensure matrix compatibility

The resulting matrix transforms multidimensional PET image data into a format suitable for functional data analysis techniques, particularly Simultaneous Confidence Corridors computation.

Typically follows databaseCreator and precedes meanNormalization in the neuroSCC analysis pipeline.

#### Value

A matrix where each row represents the PET data from one subject, formatted as a continuous line of data points.

## See Also

databaseCreator for creating the input database meanNormalization for subsequent data normalization

#### **Examples**

```
# Assuming 'database_CN', 'pattern', and 'paramZ' are defined
SCC_CN <- matrixCreator(database_CN, pattern, paramZ = 35)</pre>
```

meanNormalization

Mean Average Normalization for Matrix Data

#### **Description**

This function normalizes each row of the given matrix by its mean value. It divides each element in a row by the mean of that row, ignoring NA values. This normalization is a critical pre-processing step when comparing data from multiple sources to account for global intensity differences.

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#### Usage

```
meanNormalization(
  matrixData,
  handleInvalidRows = c("warn", "error", "omit"),
  returnDetails = FALSE,
  quiet = FALSE
)
```

#### **Arguments**

matrixData

matrix, a matrix where each row represents data that needs to be normalized, typically the output from matrixCreator.

handleInvalidRows

character, specifies how to handle rows with invalid means (zero or NA). Options are: "warn" (default) warns and leaves row unnormalized, "error" stops with an error, or "omit" removes problematic rows from the result.

returnDetails

logical, if TRUE, returns a list containing the normalized matrix and additional diagnostic information. If FALSE (default), returns only the normalized matrix.

quiet

logical, if TRUE, suppresses console messages. Default is FALSE.:

#### **Details**

The function iterates over each row of the input matrix, calculates the mean of the row, and then divides each element of the row by the calculated mean. This process adjusts for global intensity differences between rows in the matrix.

In addition to normalization, the function performs statistical analysis on row means to identify potential outliers that might indicate data quality issues. Outlier detection uses the Interquartile Range (IQR) method with thresholds at 1.5xIQR and 3xIQR.

This function is typically used after matrixCreator in the neuroSCC workflow.

#### Value

If returnDetails=FALSE (default), returns a matrix where each row has been normalized by its mean value. If returnDetails=TRUE, returns a list containing:

- normalizedMatrix: The normalized matrix
- rowMeans: Vector of all calculated row means
- problemRows: Indices of rows with invalid means
- outlierRows: Indices of statistical outliers (based on 1.5*IQR*) \item extremeOutlierRows: Indices of extreme outliers (based on 3IQR)
- summary: Count of normal vs. problematic rows and thresholds used

#### See Also

matrixCreator for creating the data matrix to be normalized.

ImageSCC::scc2g.image for computing Simultaneous Confidence Corridors for the difference between groups using the normalized matrices of each group.

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#### **Examples**

```
## Not run:
# In a typical workflow:
# Assuming data matrices already created with matrixCreator
matrixCN <- matrixCreator(database_CN, pattern, paramZ = 35)
matrixAD <- matrixCreator(database_AD, pattern, paramZ = 35)

# Basic usage - just normalize the matrices
matrixCN <- meanNormalization(matrixCN)
matrixAD <- meanNormalization(matrixAD)

# Advanced usage - get detailed diagnostics
results <- meanNormalization(matrixCN, returnDetails = TRUE)
normalizedMatrix <- results$normalizedMatrix

# Remove problematic rows automatically
cleanMatrix <- meanNormalization(matrixCN, handleInvalidRows = "omit")
## End(Not run)</pre>
```

neuroCleaner

Clean and load data from NIFTI neuroimaging files

#### **Description**

Loads a NIFTI-format neuroimaging file, converts it to a structured data frame, and organizes the data for further analysis. This function serves as the first step in the neuroimaging data processing pipeline, transforming raw PET data into a format suitable for functional data analysis. The neuroSCC package prepares and organizes neuroimaging data, while the actual Simultaneous Confidence Corridors (SCCs) are computed using functions from the ImageSCC package such as ImageSCC::scc1g.image or ImageSCC::scc2g.image.

## Usage

```
neuroCleaner(name, demo = NULL, demoRow = 1)
```

#### **Arguments**

name A character string specifying the path to the NIFTI file.

demo An optional data frame containing demographic information for the participants.

If provided, it should contain columns that match (case-insensitive): 'PPT', 'Group', 'Sex', and 'Age'. The 'PPT' column can contain participant IDs that match the name parameter for automatic matching, but if no match is found, the

row specified by demoRow will be used. Default is NULL.

demoRow An integer specifying which row of the demographic data to use when automatic

matching fails or multiple matches are possible. Default is 1.

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#### **Details**

The function performs several key operations:

- 1. Reads the NIFTI file using oro.nifti package functions
- 2. Converts the 3D image data to a structured data frame
- 3. Extracts the dimensional information (z, x, y coordinates)
- 4. Organizes the PET intensity values
- 5. If demographic data is provided, merges it with the image data

The resulting data frame serves as input for subsequent analysis functions in the neuroSCC pipeline, such as databaseCreator and matrixCreator, which prepare the data for eventual analysis with the ImageSCC package functions.

#### Value

A data frame with the following columns:

- If demographic data provided: PPT, Group, Sex, Age, z, x, y, pet
- If no demographic data: z, x, y, pet

Each row represents a voxel (3D pixel) from the image, with pet containing the intensity value at that location.

#### See Also

databaseCreator for creating databases from multiple NIFTI files.
oro.nifti::readNIfTI for the underlying function used to read NIFTI files.

## **Examples**

```
# Example 1: Using package sample data
## Not run:
# Access sample files included with the package
data_dir <- system.file("extdata", package = "neuroSCC")</pre>
nifti_file <- file.path(data_dir, "sampleFile1.nii")</pre>
# Basic usage with just a NIFTI file
pet_data <- neuroCleaner(nifti_file)</pre>
# Display the first few rows of the result
head(pet_data)
    z x y
                 pet
    1 1 1 0.00000
    1 1 2 0.00000
#>
    1 1 3 0.78526
#>
#>
# Example 2: With demographic data
# Load demographic data
demo_file <- file.path(data_dir, "Demographics.csv")</pre>
demo_data <- read.csv(demo_file)</pre>
# Display the demographic data
print(demo_data)
```

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```
PPT Group Sex Age
#> 1 041_S_1391
                   AD M 85
#> 2 036_S_1001
                   AD
                        M 69
#> 3 037_S_0627
                   ΑD
                       F 59
# Process the first NIFTI file with demographic data
# This will attempt to match based on filename
pet_with_demo <- neuroCleaner(nifti_file, demo = demo_data)</pre>
# Display the first few rows with demographic information
head(pet_with_demo)
#>
           PPT Group Sex Age z x y
#> 041_S_1391
                 AD M 85 1 1 1 0.00000
#> 041_S_1391
                  AD M 85 1 1 2 0.00000
#> 041_S_1391
                  AD M 85 1 1 3 0.78526
#> ...
# Example 3: Using a specific row from demographic data
# Process another NIFTI file and specify which demographic row to use
nifti_file2 <- file.path(data_dir, "sampleFile2.nii")</pre>
pet_with_specific_demo <- neuroCleaner(nifti_file2, demo = demo_data, demoRow = 3)</pre>
# Display the first few rows (now with demographic info from row 3)
head(pet_with_specific_demo)
          PPT Group Sex Age z x y
#>
#> 037_S_0627
                AD F 59 1 1 1 0.00000
                  AD F 59 1 1 2 0.00000
#> 037_S_0627
#> 037_S_0627
                 AD F 59 1 1 3 0.78526
#> ...
## End(Not run)
# Example 4: Creating synthetic data (fully reproducible)
# Create a simple 3D array as a synthetic NIFTI image
if (requireNamespace("oro.nifti", quietly = TRUE)) {
  # Temporary file path
  temp_nii <- tempfile(fileext = ".nii")</pre>
  # Create a small synthetic NIFTI file (3x3x3)
  img_data <- array(1:27, dim = c(3, 3, 3))
  nii_obj <- oro.nifti::nifti(img_data)</pre>
  oro.nifti::writeNIfTI(nii_obj, filename = temp_nii, verbose = FALSE)
  # Sample demographic data
  demo_data <- data.frame(</pre>
   PPT = c("sample001", "sample002", "sample003"),
Group = c("Control", "Patient", "Patient"),
    Sex = c("M", "F", "M"),
    Age = c(65, 70, 75)
  # Process the synthetic NIFTI with demographic data (use row 2)
  # This will not run if oro.nifti is not installed
  pet_data <- neuroCleaner(temp_nii, demo = demo_data, demoRow = 2)</pre>
  head(pet_data)
}
```

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neuroContour	Obtain and save neuroimaging contours from a NIFTI file

#### **Description**

This function extracts contours from a neuroimaging NIFTI file where values change according to specified levels. It processes the NIFTI file with neuroCleaner to extract structured neuroimaging data, then extracts contours using contoureR::getContourLines. These contours serve as input for Triangulation::TriMesh, which is used in Simultaneous Confidence Corridors (SCCs) calculations.

While **not mandatory**, it is **highly recommended** that the input NIFTI file be pre-processed such that zero values represent the background and non-zero values represent regions of interest. The function's default behavior extracts contours at level 0, which is ideal for well-masked data.

## Usage

```
neuroContour(niftiFile, paramZ = 35, levels = c(0), plotResult = FALSE)
```

#### **Arguments**

niftiFile	character, the path to the NIFTI file containing neuroimaging data. Ideally, the file should be masked so that zero values represent the background.
paramZ	integer, the specific z-slice to extract contours from. Default is 35.
levels	numeric, a vector of levels at which to draw the contours. Default is c(0).
plotResult	logical, if TRUE, plots the extracted contours. Default is FALSE.

#### Details

This function extracts contours from a **NIFTI** file, typically a **masked** image where background values are set to zero, and regions of interest contain non-zero values. While users can specify a different boundary level, the recommended approach is to use levels = 0 for masked data.

The extracted contours are typically used as input to Triangulation::TriMesh to create a triangular mesh of the region, which is then used for Simultaneous Confidence Corridors calculations.

#### Value

A list of data frames, where each data frame contains the x and y coordinates of a contour. The first element typically represents the external boundary, while subsequent elements (if present) represent internal contours or holes. Each data frame has two columns:

- x: x-coordinates of the contour points
- y: y-coordinates of the contour points

#### See Also

getContourLines for the underlying contour extraction. Triangulation::TriMesh for the next step in the SCC calculation process. 14 processROIs

#### **Examples**

```
## Not run:
# Load a sample NIFTI file from the neuroSCC package
library(neuroSCC)
maskPath <- system.file("extdata", "new_mask.nii", package = "neuroSCC")

# Extract contours from z-slice 35 and automatically show plot
contours <- neuroContour(maskPath, paramZ = 35, levels = c(0), plotResult = TRUE)

# Show the first few extracted points of the external contour
head(contours[[1]])

# If internal contours exist, show them as well
if (length(contours) > 1) {
   for (j in 2:length(contours)) {
      print(head(contours[[j]])) # Show points of internal contours
   }
}

## End(Not run)
```

processROIs

Process ROIs and Save Data Tables

#### **Description**

This function processes **Regions of Interest (ROIs)** from binary NIfTI files containing manually defined hypoactive regions. It extracts voxel coordinates where pet = 1 (indicating hypoactivity) and formats them into structured .RDS tables.

The function is originally designed for the **Ph.D. thesis**: "Development of statistical methods for the analysis of neuroimage data towards early diagnosis of neurodegenerative diseases" conducted at the **University of Santiago de Compostela** by Juan A. Arias Lopez, Prof. Pablo Aguiar-Fernández, Prof. Andrew H. Kemp, & Prof. Carmen Cadarso-Suárez. However, options are provided for **other users and setups**.

## Usage

```
processROIs(
  roiDir = "~/GitHub/PhD-2024-SCC-vs-SPM-SinglePatient-vs-Group/roisNormalizadas",
  outputDir =
   "~/GitHub/PhD-2024-SCC-vs-SPM-SinglePatient-vs-Group/roisNormalizadas/tables",
  regions,
  numbers,
  filePattern = "wwwx{region}_redim_crop_squ_flipLR_newDim_C{number}.nii",
  verbose = FALSE
)
```

#### **Arguments**

roiDir character, the base directory where the ROI NIfTI files are stored. Default: "~/GitHub/PhD-2024-SCC-vs-SPM-SinglePatient-vs-Group/roisNormalizadas".

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```
character, the directory where processed ROItable_* files will be saved. Default: "~/GitHub/PhD-2024-SCC-vs-SPM-SinglePatient-vs-Group/roisNormalizadas/tables
regions character vector, specifying the ROI region names (e.g., c("w32", "w79")).

numbers integer vector, specifying the patient/control numbers (e.g., 1:16).

filePattern character, a template for the expected NIfTI filenames. Should include {region}
and {number} placeholders. Default: "wwwx{region}_redim_crop_squ_flipLR_newDim_C{number}
verbose logical, if TRUE, prints progress messages. Default: FALSE.
```

#### **Details**

- This function **extracts voxel coordinates** (x, y, z) where pet = 1 (indicating hypoactivity).
- The **default filename structure** is based on the research thesis setup but can be adjusted.
- Processed tables are saved as ROItable\_\* .RDS files for later use in SCC vs. SPM comparisons.

#### Value

This function does not return a value. It processes and saves .RDS files in outputDir.

#### **Examples**

```
## Not run:
# Process ROIs using the thesis default setup
processROIs()

# Custom example for a different dataset
processROIs(
    roiDir = "/custom/path/rois",
    outputDir = "/custom/path/tables",
    regions = c("region1", "region2"),
    numbers = 1:10,
    filePattern = "custom_prefix_{region}_sub_{number}.nii",
    verbose = TRUE
)

## End(Not run)
```

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